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(54) Title: HUMAN PROTEINS HAVING HYDROPHOBIC DOMAINS AND DNAs ENCODING THESE PROTEINS

(57) Abstract: The present invention provides human proteins having hydrophobic domains, DNAs encoding these proteins, expression vectors for these DNAs, transformed eukaryotic cells expressing these DNAs and antibodies directed to these proteins.

#### DESCRIPTION

# Human Proteins Having Hydrophobic Domains and DNAs Encoding These Proteins

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#### TECHNICAL FIELD

The present invention relates to human proteins having hydrophobic domains, DNAs encoding these proteins, expression vectors for these DNAs, eukaryotic cells expressing these DNAs and antibodies directed to these proteins. The proteins of the present invention can be employed as pharmaceuticals or as antigens for preparing antibodies directed to these proteins. The human cDNAs of the present invention can be utilized as probes for genetic diagnosis and gene sources for gene therapy. Furthermore, the cDNAs can be utilized as gene sources for producing the proteins encoded by these cDNAs in large quantities. Cells into which these genes are introduced to express secretory proteins or membrane proteins in large quantities can be utilized for detection of the corresponding receptors or ligands, screening of novel small molecule pharmaceuticals and the like. The antibodies of the present invention can be utilized for the detection, quantification, purification and the like of the proteins of the present invention.

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#### BACKGROUND ART

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Cells secrete many proteins extracellularly. These secretory proteins play important roles in the proliferation control, the differentiation induction, the material transport, the biophylaxis, and the like of the cells. Unlike intracellular proteins, the secretory proteins exert their actions outside the cells. Therefore, they can be administered in the intracorporeal manner such as the drip, and they possess hidden the injection or potentialities as pharmaceuticals. In fact, a number of human secretory proteins such as interferons, interleukins, erythropoietin, thrombolytic agents and the like are pharmaceuticals. addition, currently employed as In secretory proteins other than those described above are undergoing clinical trials for developing their use as pharmaceuticals. It is believed that the human cells produce many unknown secretory proteins. Availability of these secretory proteins as well as genes encoding them is expected to lead to development of novel pharmaceuticals utilizing them.

On the other hand, membrane proteins play important roles, as signal receptors, ion channels, transporters and the like, in the material transport and the signal transduction through the cell membrane. Examples thereof include receptors for various cytokines, ion

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channels for the sodium ion, the potassium ion, the chloride ion and the like, transporters for saccharides, amino acids and the like. The genes for many of them have already been cloned. It has been clarified that abnormalities in these membrane proteins are involved in a number of previously cryptogenic diseases. Therefore, discovery of a new membrane protein is expected to lead to elucidation of the causes of many diseases, and isolation of new genes encoding the membrane proteins has been desired.

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Heretofore, due to difficulty in the purification from human cells, many of these secretory proteins and membrane proteins have been isolated by genetic approaches. A general method is the so-called expression cloning method, in which a cDNA library is introduced into eukaryotic cells to express cDNAs, and the cells secreting, or expressing on the surface of membrane, the protein having the activity of interest are then screened. However, only genes for proteins with known functions can be cloned by using this method.

In general, a secretory protein or a membrane protein possesses at least one hydrophobic domain within the protein. After synthesis on ribosomes, such domain works as a secretory signal or remains in the phospholipid membrane to be entrapped in the membrane. Accordingly, if the existence of a highly hydrophobic domain is observed in the amino acid sequence of a protein encoded by a cDNA when the

whole base sequence of the full-length cDNA is determined, it is considered that the cDNA encodes a secretory protein or a membrane protein.

#### 5 OBJECTS OF INVENTION

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The main object of the present invention is to provide novel human proteins having hydrophobic domains, DNAs coding for these proteins, expression vectors for these DNAs, transformed eucaryotic cells that are capable of expressing these DNAs and antibodies directed to these proteins.

#### SUMMARY OF INVENTION

As the result of intensive studies, the present inventors have successfully cloned cDNAs encoding proteins having hydrophobic domains from the human full-length cDNA bank, thereby completing the present invention. Thus, the present invention provides a human protein having hydrophobic domain(s), namely a protein comprising any one of amino acid sequences selected from the group consisting of SEQ ID NOS: 1 to 10, 31 to 40, 61 to 70, 91 to 100 and 121 to 130. Moreover, the present invention provides a DNA encoding said protein, exemplified by a cDNA comprising any one of base sequences selected from the group consisting of SEQ ID NOS: 11 to 30, 41 to 60, 71 to 90, 101 to 120 and 131

to 150, an expression vector that is capable of expressing said DNA by in vitro translation or in eukaryotic cells, a transformed eukaryotic cell that is capable of expressing said DNA and of producing said protein, and an antibody directed to said protein.

This object as well as other objects and advantages of the present invention will become apparent to those skilled in the art from the following description with reference to the accompanying drawings.

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#### BRIEF DESCRIPTION OF DRAWINGS

Figure 1: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03613.

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Figure 3: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03935.

Figure 4: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10755.

Figure 5: A figure depicting the 25 hydrophobicity/hydrophilicity profile of the protein

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encoded by clone HP10760.

Figure 6: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10764.

Figure 7: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10768.

Figure 8: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10769.

Figure 9: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10784.

Figure 10:A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10786.

Figure 11:A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03727.

20 Figure 12:A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03801.

Figure 13:A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03883.

figure depicting the Figure 14: A hydrophobicity/hydrophilicity profile of protein the encoded by clone HP03913. figure depicting the Figure 15: A hydrophobicity/hydrophilicity profile of the protein 5 encoded by clone HP10753. depicting the Figure 16: A figure hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10758. figure depicting the o Figure 17: A 10 hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10771. depicting the figure Figure 18: A hydrophobicity/hydrophilicity profile of protein the encoded by clone HP10778. 15 depicting the figure Figure 19: A hydrophobicity/hydrophilicity profile of the encoded by clone HP10781. depicting figure the Figure 20:A hydrophobicity/hydrophilicity profile of the protein 20 encoded by clone HP10785. figure . depicting the Figure 21:A hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03878. the figure depicting Figure 22:A 25

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hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03884.

Figure 23:A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03934.

Figure 24: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03949.

Figure 25: A figure depicting the

10 hydrophobicity/hydrophilicity profile of the protein
encoded by clone HP03959.

Figure 26: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03983.

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Figure 28: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10775.

Figure 29: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10782.

Figure 30:A figure depicting the hydrophobicity/hydrophilicity profile of the protein.

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figure depicting Figure 31:A the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03977. figure depicting the Figure 32:A hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10649. Figure 33:A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10779. Figure 34: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10790. figure depicting Figure 35: A the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10793. figure depicting the Figure 36: A hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10794. Figure 37: A figure depicting hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10797. Figure 38: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10798.

figure

Figure 39: A

depicting

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hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10800.

Figure 40:A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10801.

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Figure 41:A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03596.

Figure 42:A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03882.

Figure 43:A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03903.

15 Figure 44: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03974.

Figure 45: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03978.

Figure 46: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10735.

Figure 47: A figure depicting the 25 hydrophobicity/hydrophilicity profile of the protein

encoded by clone HP10750.

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Figure 48: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10777.

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Figure 49: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10780.

Figure 50:A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10795.

#### DETAILED DESCRIPTION OF THE INVENTION

obtained, for example, by a method for isolating proteins from human organs, cell lines or the like, a method for preparing peptides by the chemical synthesis based on the amino acid sequence of the present invention, or a method for producing proteins by the recombinant DNA technology using the DNAs encoding the hydrophobic domains of the present invention. Among these, the method for producing proteins by the recombinant DNA technology is preferably employed. For example, the proteins can be expressed in vitro by preparing an RNA by in vitro transcription from a vector having the cDNA of the present invention, and then carrying out in vitro translation using this RNA as a

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template. Alternatively, incorporation of the translated region into a suitable expression vector by the method known in the art may lead to expression of the encoded protein in large quantities in prokaryotic cells such as *Escherichia coli* and *Bacillus subtilis*, or eukaryotic cells such as yeasts, insect cells and mammalian cells.

In the case where the protein of the present invention is produced by expressing the DNA by in vitro translation, the protein of the present invention can be produced in vitro by incorporating the translated region of this cDNA into a vector having an RNA polymerase promoter, and then adding the vector to an in vitro translation system such as a rabbit reticulocyte lysate or a wheat germ extract, which contains an RNA polymerase corresponding to the promoter. The RNA polymerase promoters are exemplified by T7, T3, SP6 and the like. The vectors containing promoters for these RNA polymerases are exemplified by pKA1, pCDM8, pT3/T7 18, pT7/3 19, pBluescript II and the like. Furthermore, the protein of the present invention can be expressed in the secreted form or the form incorporated in the microsome membrane when a canine pancreas microsome or the like is added to the reaction system.

In the case where the protein of the present invention is produced by expressing the DNA in a microorganism such as *Escherichia coli*, a recombinant

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expression vector in which the translated region of the cDNA of the present invention is incorporated into an expression vector having an origin which is capable of replicating in the microorganism, a promoter, a ribosome-binding site, a cDNA-cloning site, a terminator and the like is constructed. After transformation of the host cells with this expression vector, the resulting transformant is cultured. Thus, the protein encoded by the cDNA can be produced in large quantities in the microorganism. In this case, a protein adding an initiation codon and a termination codon in front of and behind the selected translated region and expressing the protein. Alternatively, the protein can be expressed as a fusion protein with another protein. Only the portion of the protein encoded by the cDNA can be obtained by cleaving this fusion protein with a suitable protease. The expression vectors for Escherichia coli are exemplified by the pUC series, pBluescript II, the pET expression system, the pGEX expression system and the like.

In the case where the protein of the present invention is produced by expressing the DNA in eukaryotic cells, the protein of the present invention can be produced as a secretory protein, or as a membrane protein on the surface of cell membrane, by incorporating the translated region of the cDNA into an expression vector for eukaryotic

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cells that has a promoter, a splicing region, a poly(A) addition site and the like, and then introducing the vector into the eukaryotic cells. The expression vectors are exemplified by pKA1, pED6dpc2, pCDM8, pSVK3, pMSG, pSVL, pBK-CMV, pBK-RSV, EBV vectors, pRS, pYES2 and the like. Examples of eukaryotic cells to be used in general include mammalian cultured cells such as monkey kidney COS7 cells and Chinese hamster ovary CHO cells, budding yeasts, fission yeasts, silkworm cells, and Xenopus oocytes. Any eukaryotic cells may be used as long as they are capable of expressing the proteins of the present invention. The expression vector can be introduced into the eukaryotic cells by using a method known in the art such as the electroporation method, the calcium phosphate method, the liposome method and the DEAE-dextran method.

After the protein of the present invention is expressed in prokaryotic cells or eukaryotic cells, the protein of interest can be isolated and purified from the culture by a combination of separation procedures known in the art. Examples of the separation procedures include treatment with a denaturing agent such as urea or a detergent, sonication, enzymatic digestion, salting-out or dialysis, precipitation, centrifugation, solvent ultrafiltration, gel filtration, SDS-PAGE, isoelectric focusing, ion-exchange chromatography, hydrophobic

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chromatography, affinity chromatography and reverse phase chromatography.

The proteins of the present invention also include peptide fragments (of 5 amino acid residues or more) containing any partial amino acid sequences in the amino acid sequences represented by SEQ ID NOS: 1 to 10, 31 to 40, 61 to 70, 91 to 100 and 121 to 130. These peptide fragments can be utilized as antigens for preparation of antibodies. Among the proteins of the present invention, those having the signal sequences are secreted in the form of mature proteins after the signal sequences are removed. Therefore, these mature proteins shall come within the scope of the protein of the present invention. The N-terminal amino acid sequences of the mature proteins can be easily determined by using the method for the determination of cleavage site of a signal sequence [JP-A 8-187100]. Furthermore, some membrane proteins undergo the processing on the cell surface to be converted to the secreted forms. Such proteins or peptides in the secreted forms shall also come within the scope of the protein of the present invention. In the case where sugar chain-binding sites are present in the amino acid sequences of the proteins, expression of the proteins in appropriate eukaryotic cells affords the proteins to which sugar chains are added. Accordingly, such proteins or peptides to which sugar chains are added shall also come . 5

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within the scope of the protein of the present invention.

The DNAs of the present invention include all the DNAs encoding the above-mentioned proteins. These DNAs can be obtained by using a method for chemical synthesis, a method for cDNA cloning and the like.

The cDNAs of the present invention can be cloned, for example, from cDNA libraries derived from the human cells. The cDNAs are synthesized by using poly(A) + RNAs extracted from human cells as templates. The human cells may be cells delivered from the human body, for example, by the operation or may be the cultured cells. The cDNAs can be synthesized by using any method such as the Okayama-Berg method [Okayama, H. and Berg, P., Mol. Cell. Biol. 2: 161-170 (1982)], the Gubler-Hoffman method [Gubler, U. and Hoffman, J., Gene 25: 263-269 (1983)] and the like. However, it is desirable to use the capping method [Kato, S. et al., Gene 150: 243-250 (1994)], as exemplified in Examples, in order to obtain a full-length clone in an effective manner. In addition, commercially available human cDNA libraries can be utilized. The cDNAs of the present invention can be from the CDNA libraries by synthesizing cloned oligonucleotide on the basis of base sequences of any portion in the cDNA of the present invention and screening the cDNA libraries using this oligonucleotide as a probe for colony or plaque hybridization according to a method known

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in the art. In addition, the cDNA fragments of the present invention can be prepared from an mRNA isolated from human cells by the RT-PCR method in which oligonucleotides which hybridize with both termini of the cDNA fragment of interest are synthesized, which are then used as the primers.

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The cDNAs of the present invention are characterized in that they comprise any one of the base sequences represented by SEQ ID NOS: 11 to 20, 41 to 50, 71 to 80, 101 to 110 and 131 to 140 or the base sequences represented by SEQ ID NOS: 21 to 30, 51 to 60, 81 to 90, 111 to 120 and 141 to 150. Table 1 summarizes the clone number (HP number), the cells from which the cDNA clone was obtained, the total number of bases of the cDNA, and the number of the amino acid residues of the encoded protein, for each of the cDNAs.

Table 1

| .:.<br>Sequence |     | No.  | HP No.  | Cell                 | Number | Number of |
|-----------------|-----|------|---------|----------------------|--------|-----------|
|                 |     |      |         |                      | of     | amino     |
|                 |     |      |         |                      | bases  | acids     |
| 1,              | 11, | 21   | HP03613 | Kidney               | 2865   | 578       |
| 2,              | 12, | 22   | HP03700 | Kidney               | 3323   | 243       |
| 3,              | 13, | 23   | нр03935 | Kidney               | 1585   | 461       |
| 4,              | 14, | 24   | HP10755 | Kidney               | 2122   | 647       |
| 5,              | 15, | 25   | HP10760 | Kidney               | 1775   | 446       |
| 6,              | 16, | 26   | HP10764 | Kidney               | 1372   | 197       |
| 7,              | 17, | 27   | HP10768 | Kidney               | 2074   | 540       |
| 8,              | 18, | 28   | HP10769 | Kidney               | 2252   | 442       |
| 9,              | 19, | 29   | HP10784 | Kidney               | 1461   | 262       |
| 10,             | 20, | 30   | HP10786 | Kidney               | 1122   | 152       |
| 31,             | 41, | 51   | HP03727 | Kidney               | 1617   | 335       |
| 32,             | 42, | 52   | HP03801 | Umbilical cord blood | 1749   | 208       |
| 33,             | 43, | 53   | HP03883 | Kidney               | 1402   | 406       |
| 34,             | 44, | 54   | HP03913 | Kidney               | 2474   | 618       |
| 35,             | 45, | 55   | HP10753 | Umbilical cord blood | 3296   | 208       |
| 36,             | 46, | 56   | HP10758 | Kidney               | 1818   | 502       |
| 37,             | 47, | 57   | HP10771 | Kidney               | 1646   | 336       |
| 38,             | 48, | 58   | HP10778 | Kidney               | 1416   | 340       |
| 39,             | 49, | . 59 | HP10781 | Kidney               | 1927   | 223       |
| 40,             | 50, | 60   | HP10785 | Kidney               | 1419   | 309       |
| 61,             | 71, | 81   | HP03878 | Kidney               | 2016   | 599 .     |
| 62,             | 72, | 82   | HP03884 | Kidney               | 1446   | 81        |
| 63,             | 73, | 83   | HP03934 | Kidney               | 2467   | 654       |
| 64,             | 74, | 84   | HP03949 | Kidney               | 1450   | 390       |
| 65,             | 75, | 85   | HP03959 | Kidney               | 1897   | 452       |

Table 1 (continued)

| Somiongo No   | UD No       | Coll                                  | NY1    |           |   |
|---------------|-------------|---------------------------------------|--------|-----------|---|
| Sequence No   | . HP No.    | Cell                                  | Number | Number of |   |
|               |             |                                       | of     | amino     |   |
| <del></del> - | <del></del> | · · · · · · · · · · · · · · · · · · · | bases  | acids     |   |
| 66, 76, 8     | 6 HP03983   | Kidney                                | 1856   | 490       |   |
| 67, 77., 8    | 7 HP10745   | Umbilical cord blood                  | 2173   | 392       |   |
| 68, 78, 88    | 3 HP10775   | Kidney                                | 1934   | 538       |   |
| 69, 79, 89    | 9 HP10782   | Kidney                                | 1880   | 102       |   |
| 70, 80, 90    | HP10787     | Kidney                                | 2295   | 442       |   |
| 91, 101, 113  | L HP03977   | Kidney                                | 1894   | 227       |   |
| 92, 102, 112  | P10649      | KB                                    | 2413   | 352       |   |
| 93, 103, 113  | B HP10779   | Kidney .                              | 2376   | 130       | , |
| 94, 104, 114  | HP10790     | Kidney                                | 1155   | 330       |   |
| 95, 105, 115  | HP10793     | Kidney                                | 1329   | 350       |   |
| 96, 106, 116  | HP10794     | Kidney                                | 1387   | 113       |   |
| 97, 107, 117  | HP10797     | Kidney                                | 1158   | 189       |   |
| 98, 108, 118  | HP10798     | Kidney                                | 1106   | 277       |   |
| 99, 109, 119  | HP10800     | Kidney                                | 1907   | 274       |   |
| 100, 110, 120 | HP10801     | Kidney                                | 1816   | 390       |   |
| 121, 131, 141 | HP03696     | Umbilical cord blood                  | 1961   | 395       |   |
| 122, 132, 142 | P03882      | Kidney                                | 2194   | 550       |   |
| 123, 133, 143 | нр03903     | Kidney                                | 2753   | 218       |   |
| 124, 134, 144 | HP03974     | Kidney                                | 2085   | 596 .     |   |
| 125, 135, 145 | нр03978     | Kidney                                | 2208   | 467       | • |
| 126, 136, 146 | HP10735     | Umbilical cord blood                  | 2044   | 476       |   |
| 127, 137, 147 | HP10750     | Umbilical cord blood                  | 2176   | 449       |   |
| 128, 138, 148 | HP10777     | Kidney                                | 1363   | 105       |   |
| 129, 139, 149 | HP10780     | Kidney                                | 1043   | 81        |   |
| 130, 140, 150 | HP10795     | Kidney                                | 2435   | 552       |   |

The same clones as the cDNAs of the present

invention can be easily obtained by screening the cDNA libraries constructed from the human cell lines or human tissues utilized in the present invention using an oligonucleotide probe synthesized on the basis of the base sequence of the cDNA provided in any one of SEQ ID NOS: 11 to 30, 41 to 60, 71 to 90, 101 to 120 and 131 to 150.

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In general, the polymorphism due to the individual differences is frequently observed in human genes. Accordingly, any cDNA in which one or plural nucleotides are added, deleted and/or substituted with other nucleotides in SEQ ID NOS: 11 to 30, 41 to 60, 71 to 90, 101 to 120 and 131 to 150 shall come within the scope of the present invention.

Similarly, any protein in which one or plural amino acids are added, deleted and/or substituted with other amino acids resulting from the above-mentioned changes shall come within the scope of the present invention, as long as the protein possesses the activity of the protein having any one of the amino acid sequences represented by SEQ ID NOS: 1 to 10, 31 to 40, 61 to 70, 91 to 100 and 121 to 130.

The cDNAs of the present invention also include cDNA fragments (of 10 bp or more) containing any partial base sequence in the base sequences represented by SEQ ID NOS: 11 to 20, 41 to 50, 71 to 80, 101 to 110 and 131 to 140 or in the base sequences represented by SEQ ID NOS: 21 to 30, 51 to 60, 81 to 90, 111 to 120 and 141 to 150. Also, DNA

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fragments each consisting of a sense strand and an antisense strand shall come within this scope. These DNA fragments can be utilized as the probes for the genetic diagnosis.

The antibody of the present invention can be obtained from a serum after immunizing an animal using the protein of the present invention as an antigen. A peptide that is chemically synthesized based on the amino acid sequence of the present invention and a protein expressed in eukaryotic or prokaryotic cells can be used as an antigen. Alternatively, an antibody can be prepared by introducing the above-mentioned expression vector for eukaryotic cells into the muscle or the skin of an animal by injection or by using a gene gun and then collecting a serum therefrom [JP-A 7-313187]. Animals that can be used include a mouse, a rat, a rabbit, a goat, a chicken and the like. A monoclonal antibody directed to the protein of the present invention can be produced by fusing B cells collected from the spleen of the immunized animal with myelomas to generate hybridomas.

In addition to the activities and uses described above, the polynucleotides and proteins of the present invention may exhibit one or more of the uses or biological activities (including those associated with assays cited herein) identified below. Uses or activities described for proteins of the present invention may be provided by

and as an antigen to raise anti-DNA antibodies or elicit another immune response. Where the polynucleotide encodes a protein which binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the polynucleotide can also be used in interaction trap assays (such as, for example, that described in Gyuris et al., Cell 75:791-803 (1993)) to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of the binding interaction.

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The proteins provided by the present invention can similarly be used in assay to determine biological activity, including in a panel of multiple proteins for highthroughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in assays designed to quantitatively determine levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Where the protein binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the protein can be used to identify the other protein with which binding occurs or to identify inhibitors of the binding interaction.

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Proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of being developed into reagent grade or kit format for commercialization as research products.

Methods for performing the uses listed above are well known to those skilled in the art. References disclosing such methods include without limitation "Molecular Cloning: A Laboratory Manual", 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, J., E.F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology: Guide to Molecular Cloning Techniques", Academic Press, Berger, S.L. and A.R. Kimmel eds., 1987.

#### 15 <u>Nutritional Uses</u>

Polynucleotides and proteins of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a nitrogen source and use as a source of carbohydrate. In such cases the protein or polynucleotide of the invention can be added to the feed of a particular organism or can be administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the protein or

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polynucleotide of the invention can be added to the medium in or on which the microorganism is cultured.

# Cytokine and Cell Proliferation/Differentiation Activity

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A protein of the present invention may exhibit cytokine, cell proliferation (either inducing or inhibiting) or cell differentiation (either inducing or inhibiting) activity or may induce production of other cytokines in certain cell populations. Many protein factors discovered to date, including all known cytokines, have exhibited activity in one or more factor dependent cell proliferation assays, and hence the assays serve as a convenient confirmation of cytokine activity. The activity of a protein of the present invention is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B9, B9/11, BaF3, MC9/G, M+ (preB M+), 2E8, RB5, DA1, 123, T1165, HT2, CTLL2, TF-1, Mo7e and CMK.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for T-cell or thymocyte proliferation include without limitation those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In

Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Bertagnolli et al., J. Immunol. 145:1706-1712, 1990; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Bertagnolli, et al., J. Immunol. 149:3778-3783, 1992; Bowman et al., J. Immunol. 152: 1756-1761, 1994.

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Assays for cytokine production and/or spleen cells, lymph node cells or proliferation of thymocytes include, without limitation, those described in: 4 Polyclonal T cell stimulation, Kruisbeek, A.M. and Shevach, E.M. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 3.12.1-3.12.14, John Wiley and Sons, Toronto. 1994; and Measurement of mouse and human Interferon y, Schreiber, R.D. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.8.1-6.8.8, John Wiley and Sons, Toronto. 1994.

Assays for proliferation and differentiation of hematopoietic and lymphopoietic cells include, without limitation, those described in: Measurement of Human and Murine Interleukin 2 and Interleukin 4, Bottomly, K., Davis, L.S. and Lipsky, P.E. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.3.1-6.3.12, John Wiley and Sons, Toronto. 1991; deVries et al., J. Exp. Med. 173:1205-1211, 1991; Moreau et al., Nature 336:690-692, 1988;

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Greenberger et al., Proc. Natl. Acad. Sci. U.S.A. 80:2931-2938, 1983; Measurement of mouse and human interleukin 6-Nordan, R. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.6.1-6.6.5, John Wiley and Sons, Toronto. 1991; Smith et al., Proc. Natl. Acad. Sci. U.S.A. 83:1857-1861, 1986; Measurement of human Interleukin 11 -Bennett, F., Giannotti, J., Clark, S.C. and Turner, K. J. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.15.1 John Wiley and Sons, Toronto. 1991; Measurement of mouse and human Interleukin 9 - Ciarletta, A., Giannotti, 10 J., Clark, S.C. and Turner, K.J. In Current Protocols. in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.13.1, John Wiley and Sons, Toronto. 1991.

Assays for T-cell clone responses to antigens (which will identify, among others, proteins that affect APC-T cell interactions as well as direct T-cell effects by measuring proliferation and cytokine production) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function; Chapter 6, Cytokines and their cellular receptors; Chapter 7, Immunologic studies in Humans); Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J.

11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

#### Immune Stimulating or Suppressing Activity

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A protein of the present invention may also exhibit immune stimulating or immune suppressing activity, including without limitation the activities for which assays are described herein. A protein may be useful in the treatment of various immune deficiencies and disorders (including severe combined immunodeficiency (SCID)), e.g., in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as effecting the cytolytic activity of NK cells and other cell populations. These immune deficiencies may be genetic or be caused by viral (e.g., HIV) as well as bacterial or fungal infections, or may result from autoimmune disorders. More specifically, infectious diseases causes by viral, bacterial, fungal or other infection may be treatable using a protein of the present invention, including infections by HIV, hepatitis viruses, herpesviruses, mycobacteria, Leishmania spp. and various fungal infections such malaria candidiasis. Of course, in this regard, a protein of the present invention may also be useful where a boost to the immune system generally may be desirable, i.e., in the treatment of cancer.

Autoimmune disorders which may be treated using a

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protein of the present invention include, for example, connective tissue disease, multiple sclerosis, systemic rheumatoid arthritis, autoimmune lupus erythematosus, pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, insulin dependent diabetes mellitis, myasthenia autoimmune gravis, graft-versus-host disease and inflammatory eye disease. Such a protein of the present invention may also to be useful in the treatment of allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems. Other immune is suppression desired in which conditions, (including, for example, organ transplantation), may also be treatable using a protein of the present invention.

Using the proteins of the invention it may also be possible to immune responses, in a number of ways. Down regulation may be in the form of inhibiting or blocking an response already in progress or may preventing the induction of immune response. an functions of activated T cells may be inhibited by suppressing T cell responses or by inducing specific tolerance in T cells, or both. Immunosuppression of T cell responses is generally an active, non-antigen-specific, process which requires continuous exposure of the T cells to the suppressive agent. Tolerance, which involves inducing non-responsiveness or anergy in T cells, is distinguishable WO 01/49728

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from immunosuppression in that it is generally antigenspecific and persists after exposure to the tolerizing agent
has ceased. Operationally, tolerance can be demonstrated by
the lack of a T cell response upon reexposure to specific
antigen in the absence of the tolerizing agent.

Down regulating or preventing one or more antigen functions (including without limitation B lymphocyte antigen functions (such as , for example, B7)), e.g.; preventing high level lymphokine synthesis by activated T cells, will situations of tissue, skin and organ useful in be transplantation and in graft-versus-host disease (GVHD). For example, blockage of T cell function should result in reduced tissue destruction in tissue transplantation. rejection of the transplants, tissue Typically, in transplant is initiated through its recognition as foreign by T cells, followed by an immune reaction that destroys the transplant. The administration of a molecule which inhibits or blocks interaction of a B7 lymphocyte antigen with its natural ligand(s) on immune cells (such as a soluble, monomeric form of a peptide having B7-2 activity alone or in conjunction with a monomeric form of a peptide having an activity of another B lymphocyte antigen (e.g., B7-1, B7-3) or blocking antibody), prior to transplantation can lead to the binding of the molecule to the natural ligand(s) on the immune cells without transmitting the corresponding

costimulatory signal. Blocking B lymphocyte antigen function in this matter prevents cytokine synthesis by immune cells, such as T cells, and thus acts as an immunosuppressant. Moreover, the lack of costimulation may also be sufficient to anergize the T cells, thereby inducing tolerance in a subject. Induction of long-term tolerance by B lymphocyte antigen-blocking reagents may avoid the necessity of repeated administration of these blocking reagents. To achieve sufficient immunosuppression or tolerance in a subject, it may also be necessary to block the function of a combination of B lymphocyte antigens.

The efficacy of particular blocking reagents in preventing organ transplant rejection or GVHD can be assessed using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4Ig fusion proteins in vivo as described in Lenschow et al., Science 257:789-792 (1992) and Turka et al., Proc. Natl. Acad. Sci USA, 89:11102-11105 (1992). In addition, murine models of GVHD (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be used to determine the effect of blocking B lymphocyte antigen function in vivo on the development of that disease.

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Blocking antigen function mav also be therapeutically useful for treating autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T cells that are reactive against self tissue and which promote the production of cytokines autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block costimulation of T cells by disrupting receptor: ligand interactions of B lymphocyte antigens can be 3 used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which may be involved in the disease process. Additionally, blocking reagents may induce antigen-specific tolerance autoreactive T cells which could lead to long-term relief from the disease. The efficacy of blocking reagents in preventing or alleviating autoimmune disorders can determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythmatosis in MRL/lpr/lpr mice or NZB hybrid mice, murine autoimmune collagen arthritis, diabetes mellitus in NOD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 840-856).

Upregulation of an antigen function (preferably a B lymphocyte antigen function), as a means of up regulating useful in therapy. also beresponses, may immune Upregulation of immune responses may be in the form of enhancing an existing immune response or eliciting an initial immune response. For example, enhancing an immune response through stimulating B lymphocyte antigen function may be useful in cases of viral infection. In addition, systemic viral diseases such as influenza, the common cold, and encephalitis might be alleviated by the administration of stimulatory forms of B lymphocyte antigens systemically.

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Alternatively, anti-viral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells in vitro with viral antigen-pulsed APCs either expressing a peptide of the present invention or together with a stimulatory form of a soluble peptide of the present invention and reintroducing the in vitro activated T cells into the patient. Another method of enhancing anti-viral immune responses would be to isolate infected cells from a patient, transfect them with a nucleic acid encoding a protein of the present invention as described herein such that the cells express all or a portion of the protein on their surface, and reintroduce the transfected cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to, and

thereby activate, T cells in vivo.

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regulation application, up oranother enhancement of antigen function (preferably B lymphocyte antigen function) may be useful in the induction of tumor immunity. Tumor cells (e.g., sarcoma, melanoma, lymphoma, leukemia, neuroblastoma, carcinoma) transfected with a nucleic acid encoding at least one peptide of the present invention can be administered to a subject to overcome tumor-specific tolerance in the subject. If desired, the tumor cell can be transfected to express a combination of peptides. For example, tumor cells obtained from a patient can be transfected ex vivo with an expression vector directing the expression of a peptide having B7-2-like activity alone, or in conjunction with a peptide having B7-1-like activity and/or B7-3-like activity. The transfected tumor cells are returned to the patient to result in expression of the peptides on the surface of the transfected cell. Alternatively, gene therapy techniques can be used to target a tumor cell for transfection in vivo.

The presence of the peptide of the present invention having the activity of a B lymphocyte antigen(s) on the surface of the tumor cell provides the necessary costimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor cells. In addition, tumor cells which lack MHC class I or MHC class II

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molecules, or which fail to reexpress sufficient amounts of MHC class I or MHC class II molecules, can be transfected with nucleic acid encoding all or a portion of (e.g., a cytoplasmic-domain truncated portion) of an MHC class I lphachain protein and  $\beta$ , microglobulin protein or an MHC class II  $\alpha$  chain protein and an MHC class II  $\beta$  chain protein to thereby express MHC class I or MHC class II proteins on the cell surface. Expression of the appropriate class I or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (e.g., B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which blocks expression of an MHC class II associated invariant chain, can also such as the protein, cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for thymocyte or splenocyte cytotoxicity include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan,

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A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et 5 al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 10 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Bowmanet al., J. Virology 61:1992-1998; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Brown et al., J. Immunol. 153:3079-3092, 1994. 15

Assays for T-cell-dependent immunoglobulin responses and isotype switching (which will identify, among others, proteins that modulate T-cell dependent antibody responses and that affect Th1/Th2 profiles) include, without limitation, those described in: Maliszewski, J. Immunol. 144:3028-3033, 1990; and Assays for B cell function: In vitro antibody production, Mond, J.J. and Brunswick, M. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 3.8.1-3.8.16, John Wiley and Sons, Toronto. 1994.

Mixed lymphocyte reaction (MLR) assays (which will

identify, among others, proteins that generate predominantly Th1 and CTL responses) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., J. Immunol. 149:3778-3783, 1992.

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Dendritic cell-dependent assays (which will identify, among others, proteins expressed by dendritic cells that activate naive T-cells) include, without limitation, those described in: Guery et al., J. Immunol. 134:536-544, 1995; Inaba et al., Journal of Experimental Medicine 173:549-559, 1991; Macatonia et al., Journal of Immunology 154:5071-5079, 1995; Porgador et al., Journal of Experimental Medicine 182:255-260, 1995; Nair et al., Journal of Virology 67:4062-4069, 1993; Huang et al., Science 264:961-965, 1994; Macatonia et al., Journal of 20 Experimental Medicine 169:1255-1264, 1989; Bhardwaj et al., Journal of Clinical Investigation 94:797-807, 1994; and Inaba et al., Journal of Experimental Medicine 172:631-640, 1990.

Assays for lymphocyte survival/apoptosis (which

will identify, among others, proteins that prevent apoptosis after superantigen induction and proteins that regulate lymphocyte homeostasis) include, without limitation, those described in: Darzynkiewicz et al., Cytometry 13:795-808, 1992; Gorczyca et al., Leukemia 7:659-670, 1993; Gorczyca et al., Cancer Research 53:1945-1951, 1993; Itoh et al., Cell 66:233-243, 1991; Zacharchuk, Journal of Immunology 145:4037-4045, 1990; Zamai et al., Cytometry 14:891-897, 1993; Gorczyca et al., International Journal of Oncology 1:639-648, 1992.

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Assays for proteins that influence early steps of T-cell commitment and development include, without limitation, those described in: Antica et al., Blood 84:111-117, 1994; Fine et al., Cellular Immunology 155:111-122, 1994; Galy et al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad Sci. USA 88:7548-7551, 1991.

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#### Hematopoiesis Regulating Activity

A protein of the present invention may be useful in regulation of hematopoiesis and, consequently, in the treatment of myeloid or lymphoid cell deficiencies. Even marginal biological activity in support of colony forming cells or of factor-dependent cell lines indicates involvement in regulating hematopoiesis, e.g. in supporting the growth and proliferation of erythroid progenitor cells alone or in combination with other cytokines, thereby

indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to stimulate the production of erythroid precursors and/or erythroid cells; in supporting the growth and proliferation granulocytes and such as myeloid cells 5 of traditional activity) monocytes/macrophages (i.e., CSF useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelo-suppression; in supporting megakaryocytes proliferation of and the consequently of platelets thereby allowing prevention or 10 disorders such platelet various treatment of thrombocytopenia, and generally for use in place of or complementary to platelet transfusions; and/or in supporting the growth and proliferation of hematopoietic stem cells which are capable of maturing to any and all of the above-15 mentioned hematopoietic cells and therefore find therapeutic utility in various stem cell disorders (such as those usually treated with transplantation, including, without anemia and paroxysmal nocturnal aplastic limitation, hemoglobinuria), as well as in repopulating the stem cell 20 compartment post irradiation/chemotherapy, either in-vivo or conjunction with bone ex-vivo (i.e., in progenitor cell with peripheral transplantation or transplantation (homologous or heterologous)) as normal cells or genetically manipulated for gene therapy. 25

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for proliferation and differentiation of various hematopoietic lines are cited above.

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Assays for embryonic stem cell differentiation (which will identify, among others, proteins that influence embryonic differentiation hematopoiesis) include, without limitation, those described in: Johansson et al. Cellular Biology 15:141-151, 1995; Keller et al., Molecular and Cellular Biology 13:473-486, 1993; McClanahan et al., Blood 81:2903-2915, 1993.

Assays for stem cell survival and differentiation (which will identify, among others, proteins that regulate lympho-hematopoiesis) include, without limitation, those described in: Methylcellulose colony forming assays, Freshney, M.G. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 265-268, Wiley-Liss, Inc., New York, NY. 1994; Hirayama et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992; Primitive hematopoietic colony forming cells with high proliferative potential, McNiece, I.K. and Briddell, R.A. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 23-39, Wiley-Liss, Inc., New York, NY. 1994; Neben et al., Experimental Hematology 22:353-359, 1994; Cobblestone area forming cell assay,

Ploemacher, R.E. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 1-21, Wiley-Liss, Inc., New York, NY. 1994; Long term bone marrow cultures in the presence of stromal cells, Spooncer, E., Dexter, M. and Allen, T. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 163-179, Wiley-Liss, Inc., New York, NY. 1994; Long term culture initiating cell assay, Sutherland, H.J. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 139-162, Wiley-Liss, Inc., New York, NY. 1994.

#### Tissue Growth Activity

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A protein of the present invention also may have utility in compositions used for bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration, as well as for wound healing and tissue repair and replacement, and in the treatment of burns, incisions and ulcers.

A protein of the present invention, which induces cartilage and/or bone growth in circumstances where bone is not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Such a preparation employing a protein of the invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. De novo bone formation induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial

defects, and also is useful in cosmetic plastic surgery.

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A protein of this invention may also be used in the treatment of periodontal disease, and in other tooth repair processes. Such agents may provide an environment to attract bone-forming cells, stimulate growth of bone-forming cells or induce differentiation of progenitors of bone-forming cells. A protein of the invention may also be useful in the treatment of osteoporosis or osteoarthritis, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes.

Another category of tissue regeneration activity that may be attributable to the protein of the present invention is tendon/ligament formation. A protein of the present invention, which induces tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a tendon/ligament-like tissue inducing protein may have prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and in repairing defects to tendon or ligament tissue. De novo

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tissue formation induced by tendon/ligament-like composition of the present invention contributes to the repair of congenital, trauma induced; or other tendon or ligament defects of other origin, and is also useful in cosmetic plastic surgery for attachment or repair of tendons or ligaments. The compositions of the present invention may provide an environment to attract tendon or ligament-forming cells, stimulate growth of tendon- or ligament-forming cells, differentiation of progenitors of tendoninduce ligament-forming cells, or induce growth of tendon/ligament cells or progenitors ex vivo for return in vivo to effect tissue repair. The compositions of the invention may also be useful in the treatment of tendinitis, carpal tunnel or ligament defects. The and other tendon syndrome compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well known in the art.

The protein of the present invention may also be for proliferation of neural cells useful regeneration of nerve and brain tissue, i.e. for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve tissue. More specifically, a protein may be used in the treatment of diseases of the peripheral injuries, peripheral nerve nervous system, such as

peripheral neuropathy and localized neuropathies, and central nervous system diseases, such as Alzheimer's, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome. Further conditions which may be treated in accordance with the present invention include mechanical and traumatic disorders, spinal cord disorders, head trauma such as cerebrovascular diseases such as stroke. Peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a protein of the invention.

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Proteins of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds and the like.

It is expected that a protein of the present invention may also exhibit activity for generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac) and vascular (including vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring to allow normal tissue to regenerate. A

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protein of the invention may also exhibit angiogenic activity.

A protein of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokine damage.

A protein of the present invention may also be useful for promoting or inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for tissue generation activity include, without limitation, those described in: International Patent Publication No. W095/16035 (bone, cartilage, tendon); International Patent Publication No. W095/05846 (nerve, neuronal); International Patent Publication No. W091/07491 (skin, endothelium).

Assays for wound healing activity include, without limitation, those described in: Winter, Epidermal Wound Healing, pps. 71-112 (Maibach, HI and Rovee, DT, eds.), Year Book Medical Publishers, Inc., Chicago, as modified by Eaglstein and Mertz, J. Invest. Dermatol 71:382-84 (1978).

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A protein of the present invention may also exhibit activin- or inhibin-related activities. Inhibins are characterized by their ability to inhibit the release of follicle stimulating hormone (FSH), while activins and are characterized by their ability to stimulate the release of follicle stimulating hormone (FSH). Thus, a protein of the present invention, alone or in heterodimers with a member of the inhibin  $\alpha$  family, may be useful as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals. Administration of sufficient amounts of other inhibins can induce infertility in these mammals. Alternatively, the protein of the invention, as a homodimer or as a heterodimer with other protein subunits of the inhibin- $\beta$  group, may be useful as a fertility inducing therapeutic, based upon the ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, United States Patent 4,798,885. A protein of the invention may also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime reproductive performance of domestic animals such as cows, sheep and pigs.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for activin/inhibin activity include,

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without limitation, those described in: Vale et al., Endocrinology 91:562-572, 1972; Ling et al., Nature 321:779-782, 1986; Vale et al., Nature 321:776-779, 1986; Mason et al., Nature 318:659-663, 1985; Forage et al., Proc. Natl. Acad. Sci. USA 83:3091-3095, 1986.

# Chemotactic/Chemokinetic Activity

A protein of the present invention may have chemotactic or chemokinetic activity (e.g., act as a chemokine) for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, and/or endothelial epithelial eosinophils, Chemotactic and chemokinetic proteins can be used to mobilize or attract a desired cell population to a desired site of action. Chemotactic or chemokinetic proteins provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction lymphocytes, of monocytes or neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or indirectly, the directed orientation or movement of such cell population. Preferably, the protein or peptide has the ability to directly stimulate directed movement of cells.

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Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing such protein or peptide in any known assay for cell chemotaxis.

5 The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis) consist of assays that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W.Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 6.12, Measurement of alpha and beta Chemokines 6.12.1-6.12.28; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Muller et al Eur. J. Immunol. 25: 1744-1748; Gruber et al. J. of Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol. 153: 1762-1768, 1994.

# Hemostatic and Thrombolytic Activity

A protein of the invention may also exhibit hemostatic or thrombolytic activity. As a result, such a

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protein is expected to be useful in treatment of various coagulation disorders (including hereditary disorders, such as hemophilias) or to enhance coagulation and other hemostatic events in treating wounds resulting from trauma, surgery or other causes. A protein of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as, for example, infarction of cardiac and central nervous system vessels (e.g., stroke)).

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assay for hemostatic and thrombolytic activity include, without limitation, those described in: Linet et al., J. Clin. Pharmacol. 26:131-140, 1986; Burdick et al., Thrombosis Res. 45:413-419, 1987; Humphrey et al., Fibrinolysis 5:71-79 (1991); Schaub, Prostaglandins 35:467-474, 1988.

## Receptor/Ligand Activity

demonstrate activity as receptors, receptor ligands or inhibitors or agonists of receptor/ligand interactions.

Examples of such receptors and ligands include, without limitation, cytokine receptors and their ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptor phosphatases and their ligands, receptor phosphatases and their

their ligands (including without limitation, cellular adhesion molecules (such as selectins, integrins and their ligands) and receptor/ligand pairs involved in antigen presentation, antigen recognition and development of cellular and humoral immune responses). Receptors and ligands are also useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein of the present invention (including, without limitation, fragments of receptors and ligands) may themselves be useful as inhibitors of receptor/ligand interactions.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for receptor-ligand activity include without limitation those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W.Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 7.28, Measurement of Cellular Adhesion under static conditions 7.28.1-7.28.22), Takai et al., Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987; Bierer et al., J. Exp. Med. 168:1145-1156, 1988; Rosenstein et al., J. Exp. Med. 169:149-160 1989; Stoltenborg et al., J. Immunol. Methods 175:59-68, 1994; Stitt et al., Cell 80:661-670, 1995.

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Proteins of the present invention may also exhibit anti-inflammatory activity. The anti-inflammatory activity may be achieved by providing a stimulus to cells involved in the inflammatory response, by inhibiting or promoting cellcell interactions (such as, for example, cell adhesion), by inhibiting or promoting chemotaxis of cells involved in the inflammatory process, inhibiting or promoting extravasation, or by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response. Proteins exhibiting such activities can be used to treat inflammatory conditions including chronic or acute conditions), including without limitation inflammation associated with infection (such as septic shock, sepsis or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis, hyperacute rejection, nephritis, complement-mediated cytokine or chemokine-induced lung injury, inflammatory bowel disease, Crohn's disease or resulting from over production of cytokines such as TNF or IL-1. Proteins of the invention may also be useful to treat anaphylaxis and hypersensitivity to an antigenic substance or material.

### Tumor Inhibition Activity

In addition to the activities described above for immunological treatment or prevention of tumors, a protein

of the invention may exhibit other anti-tumor activities. A protein may inhibit tumor growth directly or indirectly (such as, for example, via ADCC). A protein may exhibit its tumor inhibitory activity by acting on tumor tissue or tumor precursor tissue, by inhibiting formation of tissues necessary to support tumor growth (such as, for example, by inhibiting angiogenesis), by causing production of other factors, agents or cell types which inhibit tumor growth, or by suppressing, eliminating or inhibiting factors, agents or cell types which promote tumor growth.

#### Other Activities

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A protein of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast augmentation or diminution, change in bone form or shape); effecting biorhythms or cardiac cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization,

storage or elimination of dietary fat, lipid, protein, carbohydrate, vitamins, minerals, cofactors or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), 5 depression (including depressive disorders) and violent  $^{\circ}$ behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of embryonic stem cells in lineages other than hematopoietic lineages; hormonal or endocrine activity; in the case of 10 enzymes, correcting deficiencies of the enzyme and treating deficiency-related diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulinlike activity (such as, for example, the ability to bind antigens or complement); and the ability to act as an 15 antigen in a vaccine composition to raise an immune response against such protein or another material or entity which is cross-reactive with such protein.

#### Examples

20 The present invention is specifically illustrated in more detail by the following Examples, but Examples are not intended to restrict the present invention. The basic procedures with regard to the recombinant DNA and the enzymatic reactions were carried out according to the

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literature ["Molecular Cloning. A Laboratory Manual", Cold Spring Harbor Laboratory, 1989]. Unless otherwise stated, restriction enzymes and various modifying enzymes to be used were those available from Takara Shuzo. The buffer compositions and the reaction conditions for each of the enzyme reactions were as described in the attached instructions. The cDNA synthesis was carried out according to the literature [Kato, S. et al., Gene 150: 243-250 (1994)].

(1) Selection of cDNAs Encoding Proteins Having Hydrophobic Domains

The cDNA library of epidermoid carcinoma cell line KB (WO98/11217), and the cDNA libraries constructed from human kidney mRNA (Clontech) and human umbilical cord blood mRNA were used as cDNA libraries.

Full-length cDNA clones were selected from the respective libraries and the whole base sequences thereof were determined to construct a homo-protein cDNA bank consisting of the full-length cDNA clones. The hydrophobicity/hydrophilicity profiles were determined for the proteins encoded by the full-length cDNA clones registered in the homo-protein cDNA bank by the Kyte-Doolittle method [Kyte, J. & Doolittle, R. F., J. Mol. Biol. 157: 105-132 (1982)] to examine the presence or absence of a hydrophobic domain. A clone that has a hydrophobic region

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being assumed as a secretory signal or a transmembrane domain in the amino acid sequence of the encoded protein was selected as a clone candidate.

(2) Protein Synthesis by In Vitro Translation

The plasmid vector bearing the cDNA of the present invention was used for in vitro transcription/translation with a  $T_{\text{\tiny N}}T$  rabbit reticulocyte lysate kit (Promega). In this case, [35]methionine was added to label the expression product with a radioisotope. Each of the reactions was carried out according to the protocols attached to the kit. Two micrograms of the plasmid was subjected to the reaction at 30°C for 90 minutes in the reaction solution of a total volume of 25  $\mu$ l containing 12.5  $\mu$ l  $\mu$  of  $T_NT$  rabbit reticulocyte lysate, 0.5 µl of a buffer solution (attached to the kit), 2 µl of an amino acid mixture (without methionine),  $2 \mu l$  of [35S]methionine (Amersham) (0.37 MBq/ $\mu l$ ), 0.5 µl of T7 RNA polymerase, and 20 U of RNasin. The experiment in the presence of a membrane system was carried out by adding 2.5 µl of a canine pancreas microsome fraction (Promega) to the reaction system. 2 µl of the SDS sampling buffer (125 mM Tris-hydrochloride buffer, pH 6.8, 120 mM 2mercaptoethanol, 2% SDS solution, 0.025% Bromophenol Blue and 20% glycerol) was added to 3 µl of the reaction solution. The resulting mixture was heated at 95°C for 3 minutes and then subjected to SDS-polyacrylamide gel electrophoresis.

The molecular weight of the translation product was determined by carrying out the autoradiography.

### (3) Expression in COS7

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vector for the protein of the present invention were cultured at 37°C for 2 hours in 2 ml of the 2 x YT culture medium containing 100  $\mu$ g/ml of ampicillin, the helper phage M13K07 (50  $\mu$  1) was added thereto, and the cells were then cultured at 37°C overnight. Single-stranded phage particles were obtained by polyethylene glycol precipitation from a supernatant separated by centrifugation. The particles were suspended in 100  $\mu$ l of 1 mM Tris-0.1 mM EDTA, pH 8 (TE).

The cultured cells derived from monkey kidney, COS7, were cultured at 37°C in the presence of 5% CO<sub>2</sub> in the Dulbecco's modified Eagle's medium (DMEM) containing 10% fetal calf serum. 1 x 10<sup>5</sup> COS7 cells were inoculated into a 6-well plate (Nunc, well diameter: 3 cm) and cultured at 37°C for 22 hours in the presence of 5% CO<sub>2</sub>. After the medium was removed, the cell surface was washed with a phosphate buffer solution followed by DMEM containing 50 mM Trishydrochloride (pH 7.5) (TDMEM). A suspension containing 1 µl of the single-stranded phage suspension, 0.6 ml of the DMEM medium and 3 µl of TRANSFECTAM<sup>TM</sup> (IBF) was added to the cells and the cells were cultured at 37°C for 3 hours in the presence of 5% CO<sub>2</sub>. After the sample solution was removed,

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the cell surface was washed with TDMEM, 2 ml per well of DMEM containing 10% fetal calf serum was added, and the cells were cultured at 37°C for 2 days in the presence of 5% CO<sub>2</sub>. After the medium was exchanged for a medium containing [35S]cysteine or [35S]methionine, the cells were cultured for one hour. After the medium and the cells were separated each other by centrifugation, proteins in the medium fraction and the cell membrane fraction were subjected to SDS-PAGE.

## (4) Preparation of Antibodies

A plasmid vector containing the cDNA of the present invention was dissolved in a phosphate buffer solution (PBS: 145 mM NaCl, 2.68 mM KCl, 8.09 mM Na, HPO,, 2 mM KH,PO4, pH 7.2) at a concentration of 2  $\mu$ g/ $\mu$ l. 25  $\mu$ l each (a total of 50 µl) of the thus prepared plasmid solution in PBS was injected into the right and left musculi quadriceps femoris of three mice (ICR line) using a 26 guage needle. After similar injections were repeated for one month at intervals of one week, blood was collected. The collected blood was stored at 4°C overnight to coagulate the blood, and then centrifuged at 8,000 x g for five minutes to obtain a supernatant. NaN, was added to the supernatant to a concentration of 0.01% and the mixture was then stored at 4°C. The generation of an antibody was confirmed by immunostaining of COS7 cells into which the corresponding vector had been introduced, or by Western blotting using a

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cell lysate or a secreted product.

(5) Clone Examples

<HP03613> (SEQ ID NOS: 1, 11, and 21)

Determination of the whole base sequence of the cDNA insert of clone HP03613 obtained from cDNA library of human kidney revealed the structure consisting of a 337-bp 5'-untranslated region, a 1737-bp ORF, and a 791-bp 3'untranslated region. The ORF encodes a protein consisting of 578 amino acid residues and there existed eleven putative the 1 depicts Figure domains. transmembrane hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. translation resulted in formation of a translation product of high molecular weight.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to mouse organic cation transporter-like protein (Accession No. BAA23875). Table 2 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and mouse organic cation transporter-like protein (MT). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology

of 70.4% in the entire region.

Table 2

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- HP ASILGSLSPEALLAISIPPGPNQRPHQCRRFRQPQWQLLDPNATATSWSEADTEPCVDGW

  \*\*\* \*.\*. \*\*\* \*\*\*\* \*\*\*\* \*\*\*\*\*\*\*\* .. \*\*\*\*\* \*\*\* \*\*\*

  MT ASIPGDLGPDVLLAVSIPPGPDQQPHQCLRFRQPQWQLTESNATATNWSDAATEPCEDGW
- - MT LLVSVSGTAAAFMPTFPLYCLFRFLLASAVAGVMMNTAS----

25 HP SWWLAESARWLLTTGRLDWGLQELWRVAAINGKGAVQDTLTPEVLLSAMREELSMGQPPA

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI792236). However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

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## <HP03700> (SEQ ID NOS: 2, 12, and 22)

Determination of the whole base sequence of the cDNA insert of clone HP03700 obtained from cDNA library of human kidney revealed the structure consisting of a 45-bp 5'-untranslated region, a 732-bp ORF, and a 2546-bp 3'untranslated region. The ORF encodes a protein consisting of 243 amino acid residues and there existed three putative transmembrane 2 depicts domains. Figure hydrophobicity/hydrophilicity profile, obtained by the Kyteof the present protein. Doolittle method, translation resulted in formation of a translation product of 27 kDa that was somewhat larger than the molecular weight of 25,561 predicted from the ORF.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to mouse yolk sac permease-like molecule 1 (Accession No. AAA92292). Table 3 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and mouse yolk sac permease-like molecule 1 (MY). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 74.5% in the N-terminal region of 231 amino acid residues.

Table 3

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20 HP SGGVWGD

MY LGSCQIPLCSWRPSSTSTHICIPVFRLLSVLAPVACVWFISAFVGTSVIPLQLSEPSDAP

The search of the GenBank using the base sequences
of the present cDNA has revealed the registration of

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sequences that shared a homology of 90% or more (for example, Accession No. AW167520). However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03935> (SEQ ID NOS: 3, 13, and 23)

Determination of the whole base sequence of the cDNA insert of clone HP03935 obtained from cDNA library of human kidney revealed the structure consisting of a 72-bp 5'-untranslated region, a 1386-bp ORF, and a 127-bp 3'untranslated region. The ORF encodes a protein consisting of 461 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 3 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. translation resulted in formation of a translation product of 56 kDa that was somewhat larger than the molecular weight of 52,052 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 61 kDa. In addition, there exists in the amino acid sequence of this protein two sites at which N-glycosylation may occur (Asn-Ser-Ser at position 193 and Asn-Ser-Thr at position 236). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from histidine at position 32.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to Arabidopsis thaliana hypothetical protein (Accession No. CAB41318). Table 4 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and Arabidopsis thaliana hypothetical protein (AT). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 30.8% in the intermediate region of 214 amino acid residues.

15 Table 4

HP MAPQSLPSSRMAPLGMLLGLLMAACFTFCLSHQNLKEFALTNPEKSSTKETERKETKAEE

HP ELDAEVLEVFHPTHEWQALQPGQAVPAGSHVRLNLQTGEREAKLQYEDKFRNNLKGKRLD

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AT MPTIFFFRYVFLLVVISLVGFSIAEKVNSSGGMVWSSVRDEAELVEDSGVVIGEQDQ

 $HP \quad INTNTYTSQDLKSALAKFKEGAEMESSKEDKARQAEVKRLFRPIEELKKDFDELNVVIET$ 

. \*.... .\* .. . . \* .. \*\*\*. ..\*. . .

25 AT IDGGFSSLDGMLHWAIGHSDPATLKEAAKDAEKMS-LDELQKRQLELKELVEKLK--MPS

| :  | HP | ${\tt DMQIMVRLINKFNSSSSSLEEKIAALFDLEYYVHQMDNAQDLLSFGGLQVVINGLNSTEP}$  |
|----|----|---|
|    | •  | * * * ** *** * * *** * ** **  |
|    | AT | ${\tt NAKLMQIAIDDLNNSSLSLEDRHRALQELLILVEPIDNANDLSKSGGLRVVAGELNHDDT}$  |
| 5  |    |   |
|    | НР | $\verb LVKEYAAFVLGAAFSSNPKVQVEAIEGGALQKLLVILATEQPLTAKKKVLFALCSLLRHF $ |
|    |    | * **. *** * . ** ** * *** . *   |
|    | AT | EVRKLAAWVLGKASQNNPFVQEQVLELGALTT-LIKMVNSSSTEEAVKALFAVSALIRNN          |
|    |    |   |
| 10 | НР | PYAQRQFLKLGGLQVLRTLVQEKGTEV-LAVRVVTLLYDLVTEKMFAEEEAELTQEMSPE          |
|    |    | .* *. * .** ** ****.  |
|    | AT | IAGQDLFFAAHGYIMLRDVMNNGSLDMKLRRKAVFLVGDLAESQLQNTEKDELPIFKDRL          |
|    |    |   |
|    | НР | KLQQYRQVHLLPGLWEQGWCEITAHLLALPEHDAREKVLQTLGVLLTTCRDRYRQDPQLG          |
| 15 |    |   |
|    | ΑT | FLKSVVDLIVVLDLDLQEKALTAIQTLLQLKSIEPQVLKESCGLEEALERMKLQLEESMA          |
|    |    |   |
|    | HP | RTLASLQAEYQVLASLELQDGEDEGYFQELLGSVNSLLKELR                            |
|    |    |   |
| 20 | AT | DEYKRDYAADVESIRGEVELIFRQKLGLL   |

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AW025017) among ESTs. However, since they are

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partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10755> (SEQ ID NOS: 4, 14, and 24)

Determination of the whole base sequence of the cDNA insert of clone HP10755 obtained from cDNA library of human kidney revealed the structure consisting of a 55-bp 5'-untranslated region, a 1944-bp ORF, and a 123-bp 3'-untranslated region. The ORF encodes a protein consisting of 647 amino acid residues and there existed eight putative transmembrane domains. Figure 4 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human hypothetical protein KIAA0062 (Accession No. BAA06685). Table 5 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and human hypothetical protein KIAA0062 (KI). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention,

respectively. The both proteins shared a homology of 30.6% in the C-terminal region of 408 amino acid residues.

Table 5

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- HP MASLVSLELGLLLAVLVVTATASPPAGLLSLLTSGQGALDQEALGGLLNTLADRVHCTNG
- HP PCGKCLSVEDALGLGEPEGSGLPPGPVLEARYVARLSAAAVLYLSNPEGTCEDTRAGLWA
- 10 HP SHADHLLALLESPKALTPGLSWLLQRMQARAAGQTPKTACVDIPQLLEEAVGAGAPGSAG
  - KI RVYADAPAKLLLPPPAAWDLAVRLRGAEAASERQVYSVTM
  - HP GVLAALLDHVRSGSCFHALPSPQYFVDFVFQQHSSEVPMTLAELSALMQRLGVGREAHSD

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- KI KLLLLHPAFQSCLLLTLLGLWRTTPEAHASSLGAPAISAASFLQDLIHRYGEGDSLTLQQ
- HP HSHRHRGASSRDPVPLISSSNSSSVWDTVCLSARDVMAAYGLSEQAGVTPEAWAQLSPAL
- ..\*.\*. \*...\*\*\*. ..... ....\*..
- 20 KI LKALLNHLDVGVGRGNVTQHVQGHRNLSTCFSSGDLFTAHNFSEQSRIGSSELQEFCPTI

  - KI LQQLDSRACTSENQENEENEQTEEGRPSAVEVWGYGLLCVTVISLCSLLGASVVPFMK-K

|    | P GVAHYILQTFLSLAVGALTGDAVLHLTPKVLGLHTHSEEGLSPQPTWRLLAMLAGLYAFF |  |
|----|--|--|
|    | * * **. * *  |  |
|    | I TFYKRLLLYFIALAIGTLYSNALFQLIPEAFGFNPL-EDYYVSKSAVVFGGFYLFF     |  |
|    |  |  |
| 5  | P LFENLFNLLL-PRDPEDLEDGPCGHSS-HSHGGHSHGVSLQLAPSELRQPKPPHEG     |  |
|    | . **** .***.   |  |
|    | I FTEKILKILLKQKNEHHHGHSHYASESLPSKKDQEEGVMEKLQNGDLDHMIPQHCSSELD |  |
|    |  |  |
|    | P SRADLVAEESPELLNPEPRRLS-PELRLLPYMITLGDAVHNFADGLAV             |  |
| 10 | .,*.*.** ******.*.***  |  |
|    | I GKAPMVDEKVIVGSLSVQDLQASQSACYWLKGVRYSDIGTLAWMITLSDGLHNFIDGLAI |  |
|    |  |  |
|    | P GAAFASSWKTGLATSLAVFCHELPHELGDFAALLHAGLSVRQALLLNLASALTAFAGLYV |  |
|    | **. *. * * **. * *. ******* **. **.                            |  |
| 15 | I GASFTVSVFQGISTSVAILCEEFPHELGDFVILLNAGMSIQQALFFNFLSACCCYLGLAF |  |
|    |  |  |
|    | IP ALAVGVSEESEAWILAVATGLFLYVALCDMLPAMLKVRDPRPWLLFLLHNVGLLG     |  |
|    | * *. *. **. *. * ***. * **. * . * .                            |  |
|    | I GILAG-SHFSANWIFALAGGMFLYISLADMFPEMNEVCQEDERKGSILIPFIIQNLGLLT |  |
| 20 |  |  |
|    | IP GWTVLLLLSLYEDDITF   |  |
|    | *. * * *   |  |
|    | I GFTIMVVLTMYSGQIQIG   |  |

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base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA42490) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10760> (SEQ ID NOS: 5, 15, and 25)

Determination of the whole base sequence of the cDNA insert of clone HP10760 obtained from cDNA library of human kidney revealed the structure consisting of a 61-bp 5'-untranslated region, a 1341-bp ORF, and a 373-bp 3'untranslated region. The ORF encodes a protein consisting of 446 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 5 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 48 kDa that was somewhat smaller than the molecular weight of 49,468 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 50 kDa. In addition, there exists in the amino acid sequence of this protein two sites at which N-glycosylation may occur (Asn-Ala-Thr at position 144 and Asn-Ile-Ser at position 243). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal

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sequence, allows to expect that the mature protein starts from glutamic acid at position 27.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human 25 kDa trypsin inhibitor (Accession No. BAA25066). Table 6 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and human 25 kDa trypsin inhibitor (TI). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 33.5% in the intermediate region of 185 amino acid residues.

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Table 6

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MLHPETSPGRGHLLAVLLALLGTAWAEVWPPQLQEQAPMAG

20 TI MIAISAVSSALLFSLLCEASTVVLLNSTDSSPPTNNFTDIEAALKAQLDSADIPKARRKR

HP ALNRKESFLLLSLHNRLRSWVQPPAADMRRLDWSDSLAQLAQARAALCGIPTPSLASGLW
.....\*.\*\*.\*.\*.\*\*.\*\*.\*.\*\*.\*\*\*

TI YISQNDMIAILDYHNQVRGKVFPPAANMEYMVWDENLAKSAEAWAATC-IWDHG-PSYLL

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- HP RTLQVGWNMQLLPAGLASFVEVVSLWFAEGQRYSHA-AGEC-----AR-NATCTHYTQL

  \*\*...\*.\*.\*.\*.\*.\*

  TI RFLGQN-LSVRTGRYRSILQLVKPWYDEVKDYAFPYPQDCNPRCPMRCFGPMCTHYTQM
- 5 HP VWATSSQLGCGRHLCSAGQA—AI——EAF~VCAYSPGGNWEVNGKTIIPYKKGAWCSLC

  \*\*\*\*\*...\*\*. \* \* ..... \*\*.\*\* \* \*... \*\*\* \*... \*\*\* \*... \*\*\* \*

  TI VWATSNRIGCAIHTCQNMNVWGSVWRRAVYLVCNYAPKGNW—IGEA—PYKVGVPCSSC
- HP TASVSGCFKAWDHAGGLCEVPRNPCRMSCQNHGRLNISTCHCHCPPGYTGRYCQVRCSLQ

  10 ..\*.\*

### TI PPSYGGSCTDNLCFPGVTSNYLYWFK

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI792411) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10764> (SEQ ID NOS: 6, 16, and 26)

Determination of the whole base sequence of the CDNA insert of clone HP10764 obtained from cDNA library of human kidney revealed the structure consisting of a 326-bp 5'-untranslated region, a 594-bp ORF, and a 452-bp 3'-untranslated region. The ORF encodes a protein consisting of

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197 amino acid residues and there existed two putative transmembrane domains. Figure 6 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 25 kDa that was somewhat larger than the molecular weight of 21,508 predicted from the ORF.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H45965) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

15 <HP10768> (SEQ ID NOS: 7, 17, and 27)

Determination of the whole base sequence of the cDNA insert of clone HP10768 obtained from cDNA library of human kidney revealed the structure consisting of a 100-bp 5'-untranslated region, a 1623-bp ORF, and a 351-bp 3'untranslated region. The ORF encodes a protein consisting of 540 amino acid residues and there existed nine putative depicts the domains. Figure transmembrane hydrophobicity/hydrophilicity profile, obtained by the Kytethe present protein. In Doolittle method, of translation resulted in formation of a translation product of high molecular weight.

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA459236) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10769> (SEQ ID NOS: 8, 18, and 28)

Determination of the whole base sequence of the cDNA insert of clone HP10769 obtained from cDNA library of human kidney revealed the structure consisting of a 11-bp 5'-untranslated region, a 1329-bp ORF, and a 912-bp 3'untranslated region. The ORF encodes a protein consisting of 442 amino acid residues and there existed two putative Figure 8 depicts the transmembrane domains. hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 52 kDa that was somewhat larger than the molecular weight of 49,101 predicted from the ORF.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI625881) among ESTs. However, since they are

partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

## <HP10784> (SEQ ID NOS: 9, 19, and 29)

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Determination of the whole base sequence of the cDNA insert of clone HP10784 obtained from cDNA library of human kidney revealed the structure consisting of a 60-bp 5'-untranslated region, a 789-bp ORF, and a 612-bp 3'-untranslated region. The ORF encodes a protein consisting of 262 amino acid residues and there existed six putative transmembrane domains. Figure 9 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 28 kDa that was almost identical with the molecular weight of 27,551 predicted from the ORF.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to rice (Oryza sativa) hypothetical protein (Accession No. AAD39600). Table 7 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and rice hypothetical protein (OS). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that

of the protein of the present invention, respectively. The both proteins shared a homology of 40.0% in the intermediate region of 195 amino acid residues.

5 Table 7

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MTPEDPEETQPLLGPPGGSAPRGR

OS MSFRGEESGGEDGGRTASASDLRKPFLHTGSWYKMSSAGGGGGMGSRLGSSAYSLRDSSV

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- HP RVFLAAFAAALGPLSFGFALGYSSPAIPSLQRAAPPAPRLDDAAASWFGAVVTLGAAAGG
- OS SAVLCTLIVALGPIQFGFTCGFSSPTQDAI----ISDLGLTLSEFSLFGSLSNVGAMVGA
- 15 HP VLGGWLVDRAGRKLSLLLCSVPFVAGFAVITAAQDVWMLLGGRLLTGLACGVASLVAPVY

. .\* ... \*\*\* \*\*.. ..\* . \*. .\*. \*. .\*. \*\*\*\*.\*.. \*\* \* \*.\*\*\*

- OS IASGQIAEYIGRKGSLMIAAIPNIIGWLAISFAKDSSFLFMGRLLEGFGVGVISYVVPVY
- HP ISEIAYPAVRGLLGSCVQLMVVVGILLAYLAGWVLEWRWLAVLGCVPPSLMLLLMCFMPE

20 \*.\*\*\* ... \*\* \*\*\* \*\* \*... \*\* \*\* \* . \*\* \*... . \*.\*\*

- OS IAEIAPQTMRGALGSVNQLSVTIGILLAYLLGMFVPWRILSVLGILPCSILIPGLFFIPE
- HP TPRFLLTQHRRQEAAPGLVRCGHGVQHECLRRLLQADPGWPWQLLARGHLGACLCTAC

.\*\*.\* . .... \*

OS SPRWLAKMGKMEDFESSLQVLRGFETDIAVEVNEIKRSVQSSRRRTTIRFADIKQKRYSV

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AW028826) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

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<HP10786> (SEQ ID NOS: 10, 20, and 30)

Determination of the whole base sequence of the CDNA insert of clone HP10786 obtained from cDNA library of human kidney revealed the structure consisting of a 78-bp 5'-untranslated region, a 459-bp ORF, and a 585-bp 3'-untranslated region. The ORF encodes a protein consisting of 152 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 10 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 17 kDa that was almost identical with the molecular weight of 16,904 predicted from the ORF.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AW052022) among ESTs.

However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03727> (SEQ ID NOS: 31, 41, and 51)

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Determination of the whole base sequence of the cDNA insert of clone HP03727 obtained from cDNA library of human kidney revealed the structure consisting of a 254-bp 5'-untranslated region, a 1008-bp ORF, and a 355-bp 3'untranslated region. The ORF encodes a protein consisting of 335 amino acid residues and there existed one putative domain. Figure 11 depicts the transmembrane hydrophobicity/hydrophilicity profile, obtained by the Kytethe present protein. Doolittle method, of translation resulted in formation of a translation product of 41 kDa that was somewhat larger than the molecular weight of 37,999 predicted from the ORF.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to protein MG87 from diabetic rat kidney (Accession No. AAC64190). Table 8 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and protein MG87 from diabetic rat kidney (RD). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue

similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 74.2% in the entire region.

## 5 Table 8

- RD MGSSSSTALARLGLPGQPRSTWLGVAALGLAAVALGTVAWRRARPRRRRQLQQVGTVSKV

- RD WIYPIKSCKGVSVCETECTDMGLRCGKVRDRFWMVVKEDGHMITARQEPRLVLVTITLEN
- - RD NYLMLEAPGMEPIVLPIKLPSSNKIHDCRLFGLDIKGRDCGDEVARWFTSYLKTQAYRLV
- - HP NIVVTGCDAFEEDTWDELLIGSVEVKKVMACPRCILTTVDPDTGVIDRKQPLDTLKSYRL

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HP CDPSERELYKLSPLFGIYYSVEKIGSLRVGDPVYRMV

\*\*\*\* \*\* \*\*\* \*\*\*\*\*\*

RD CDPSVKSLYQSSPLFGMYFSVEKIGSLRVGDPVYRMVD

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI912794) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03801> (SEQ ID NOS: 32, 42, and 52)

Determination of the whole base sequence of the CDNA insert of clone HP03801 obtained from cDNA library of human umbilical cord blood revealed the structure consisting of a 158-bp 5'-untranslated region, a 627-bp ORF, and a 964-bp 3'-untranslated region. The ORF encodes a protein consisting of 208 amino acid residues and there existed six putative transmembrane domains. Figure 12 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 23 kDa that was almost identical with the molecular weight of 22,526 predicted from the ORF.

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The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human hypothetical protein CGI-15 (Accession No. AAD27724). Table 9 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and human hypothetical protein CGI-15 (CP). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The amino acid sequences of the two proteins were completely different each other in the N-terminal, intermediate and C-terminal regions although partial match was observed.

## 15 Table 9

- CP VLFILIFSLIFKLEELRAALVLVVLLIAGGLFMFTYKSTQFNVEGFAWCWGPRSSVAFAG
- - CP PSPRCSCRRLNSASRIPSTPCSTCSHSCSWGLFPLFAVFEGLHLSTSEKIFRFQDTGLLL
- 25 HP RVLGSLFLGGILAFGLGFSEFLLVSRTSSLTLSIAGIFKEVCTLLLAAHLLGDQISLLNW

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- CP RVLGSLFLGGILAFGLGFSEFLLVSRTSSLTLSIAGIFKEVCTLLLAAHLLGDQISLLNW
- HP LGFALCLSGISLHVALKALHSRGNPESLPEASVFCSSPCDS
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CP LGFASASREYPSTLPSKPCIPEVMVAPRP

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI741613) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

15 < HP03883> (SEQ ID NOS: 33, 43, and 53)

Determination of the whole base sequence of the cDNA insert of clone HP03883 obtained from cDNA library of human kidney revealed the structure consisting of a 59-bp 5'-untranslated region, a 1221-bp ORF, and a 122-bp 3'untranslated region. The ORF encodes a protein consisting of 406 amino acid residues and there existed eight putative Figure 13 depicts the domains. transmembrane hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product

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of high molecular weight.

The search of the protein database using the amino acid sequence of the present protein revealed that the choline/ethanolamine to human similar protein was phosphotransferase (Accession No. NP\_006081). Table 10 shows the comparison between amino acid sequences of the human invention present (HP) and of the choline/ethanolamine phosphotransferase (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 66.8% in the entire region. addition, the amino acid sequence from position 70 to position 311 of the present protein shared a homology of 98.3% with human AAPT1-like protein (Accession No. AAD44019).

Table 10

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MAAGAGAGSAPRWLRALSEPLSAAQLRRLEEHRYSAAG

\*\*\* \*\* \*\*\*\*\*

CE MSGHRSTRKRCGDSHPESPVGFGHMSTTGCVLNKLFQLPTPPLSRHQLKRLEEHRYQSAG

| CE    | RSLIEPI MOGYWEWLVRRYPSWIAPNI             | ITIIGLSINICTTILLVFYCPTATEQAPLW   | AYI |
|-------|--|----------------------------------|-----|
| L JE. | LOUGH CHEMOUS RESERVATIONS OF THE STATES | 111100011.201110011 101 11110414 |     |

- 5 CE ACACGLFIYQSLDAIDGKQARRTNSSSPLGELFDHGCDSLSTVFVVLGTCIAVQLGTNPD

- HP QYFNNFIDEYVVLWMAMVISSFDMVIYFSALCLQISRHLHLNIFKTACHQAPEQVQVLSS

  \*\*\*\*. \*\*\*\*. \* \*\*. \* \* ... \* ... \* ... \*..
  - CE QYFNSFIDEYIVLWIALVFSFFDLIRYCVSVCNQIASHLHIHVFRIKVSTAHSNHH

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example,

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Accession No. AI816449) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03913> (SEQ ID NOS: 34, 44, and 54)

Determination of the whole base sequence of the cDNA insert of clone HP03913 obtained from cDNA library of human kidney revealed the structure consisting of a 344-bp 5'-untranslated region, a 1857-bp ORF, and a 273-bp 3'untranslated region. The ORF encodes a protein consisting of 618 amino acid residues and there existed thirteen putative Figure 14 depicts domains. transmembrane hydrophobicity/hydrophilicity profile, obtained by the Kytethe present protein. In vitro Doolittle method, of translation resulted in formation of a translation product of high molecular weight.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human solute carrier family 5 (Accession No. NP\_000444). Table 11 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and human solute carrier family 5 (SC). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that

of the protein of the present invention, respectively. The both proteins shared a homology of 48.3% in the entire region.

5 Table 11

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- HP MEVKNFAVWDYVVFAALFFISSGIGVFFAIKERKKATSREFLVGGRQMSFGPVG \* .\*.\*\*\* \*\*\* .... \*... \*\*\* \*\*\* .... \*\*\* \*\*\* SC MEAVETGERPTFGAWDYGVFALMLLVSTGIGLWVGLARGGQRSAEDFFTGGRRLAALPVG

|    | HP LIMYSHFKDCDPWTSGIISAPDQLMPYFVMEIFATMPGLPGLFVACAFSGTLSTVASSIN |   |
|----|---|---|
|    | ***** * ****** ** .*****.***.*****                              |   |
|    | SC IVMFVFYTDCDPLLLGRISAPDQYMPLLVLDIFEDLPGVPGLFLACAYSGTLSTASTSIN |   |
| 5  |   |   |
|    | HP ALATVTFEDFVKSCFPHLSDKLSTWISKGLCLLFGVMCTSMAVAASVM-GGVVQASLSIH |   |
|    | *.*.** *** * *****.** *** ***.*                                 |   |
|    | SC AMAAVTVEDLIKPRLRSLAPRKLVIISKGLSLIYGSACLTVAALSSLLGGGVLQGSFTVM |   |
|    |   |   |
| 10 | HP GMCGGPMLGLFSLGIVFPFVNWKGALGGLLTGITLSFWVAIGAFIYPAPASKTWPLPLST | C |
|    | ***. ** * ** * * *. *. **. **. **                               |   |
|    | SC GVISGPLLGAFILGMFLPACNTPGVLAGLGAGLALSLWVALGATLYPPSEQTMRVLPSSA |   |
|    |   |   |
|    | HP DQCIKSNVTATGPPVLSSRPGIADTWYSISYLYYSAVGCLGCI                  |   |
| 15 | **.*. ** .*****.****.   |   |
|    | SC ARCVALSVNASGLLDPALLPANDSSRAPSSGMDASRPALADSFYAISYLYYGALGTLTTV |   |
|    |   |   |
|    | HP VAGVIISLITGRQRGEDIQPLLIRPVCNLFCFWSKKYKTLCWCGVQHDSGTEQENLENGS |   |
|    | . *** .*** *  |   |
| 20 | SC LCGALISCLTGPTKRSTLAPGLLWWDLARQTASVAPKEEVAILDDNLVKGPEELPTGNKK |   |
|    |   |   |
|    | HP ARKQGAESVLQNGLRRESLVHVPGYDPKDKSYNNMAFETTHF                   |   |
|    |   |   |
|    | SC PPGFLPTNEDRLFFLGQKELEGAGSWTPCVGHDGGRDQQETNL                  |   |
|    | ·   |   |

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI733508) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

## <HP10753> (SEQ ID NOS: 35, 45, and 55)

Determination of the whole base sequence of the cDNA insert of clone HP10753 obtained from cDNA library of human umbilical cord blood revealed the structure consisting of a 141-bp 5'-untranslated region, a 627-bp ORF, and a 2528-bp 3'-untranslated region. The ORF encodes a protein consisting of 208 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain in the inner portion. Figure 15 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 28 kDa that was somewhat larger than the molecular weight of 21,518 predicted from the ORF. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from methionine at position 32.

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PCT/JP00/09359

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AW162064) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10758> (SEQ ID NOS: 36, 46, and 56)

Determination of the whole base sequence of the cDNA insert of clone HP10758 obtained from cDNA library of human kidney revealed the structure consisting of a 25-bp 5'-untranslated region, a 1509-bp ORF, and a 284-bp 3'untranslated region. The ORF encodes a protein consisting of 502 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain in the inner portion. Figure 16 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 60 kDa that was somewhat larger than the molecular weight of 55,848 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 66 kDa. In addition, there exists in the amino acid sequence of this protein six sites at which N-glycosylation may occur (Asn-Val-Ser at position 67, Asn-Tyr-Thr at position 103, AsnWO 01/49728

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Phe-Thr at position 156, Asn-Ile-Thr at position 183, Asn-Phe-Thr at position 197 and Asn-Lys-Ser at position 283). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from alanine at position 15.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. T96740) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10771> (SEQ ID NOS: 37, 47, and 57)

Determination of the whole base sequence of the cDNA insert of clone HP10771 obtained from cDNA library of human kidney revealed the structure consisting of a 36-bp 5'-untranslated region, a 1011-bp ORF, and a 599-bp 3'-untranslated region. The ORF encodes a protein consisting of 336 amino acid residues and there existed one putative transmembrane domain at the N-terminus. Figure 17 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 41 kDa that was somewhat larger than the molecular weight

of 37,924 predicted from the ORF.

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The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human interferon- $\alpha$  induced protein (Accession No. AR053364). The C-terminal portion downstream from methionine at position 51 of the protein of the present invention matched with the C-terminal portion downstream from methionine at position 12 of human interferon- $\alpha$  induced protein. However, the putative transmembrane domain at the N-terminus observed for the protein of the present invention was not present in human interferon- $\alpha$  induced protein.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA452543) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10778> (SEQ ID NOS: 38, 48, and 58)

Determination of the whole base sequence of the cDNA insert of clone HP10778 obtained from cDNA library of human kidney revealed the structure consisting of a 173-bp 5'-untranslated region, a 1023-bp ORF, and a 220-bp 3'-untranslated region. The ORF encodes a protein consisting of 340 amino acid residues and there existed six putative

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transmembrane domains. Figure 18 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA429745) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10781> (SEQ ID NOS: 39, 49, and 59)

Determination of the whole base sequence of the CDNA insert of clone HP10781 obtained from cDNA library of human kidney revealed the structure consisting of a 88-bp 5'-untranslated region, a 672-bp ORF, and a 1167-bp 3'-untranslated region. The ORF encodes a protein consisting of 223 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 19 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 31 kDa that was larger than the molecular weight of 24,239 predicted from the ORF. In this case, the addition of

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a microsome led to the formation of a product of 33 kDa. In addition, there exists in the amino acid sequence of this protein two sites at which N-glycosylation may occur (Asn-Asn-Thr at position 70 and Asn-Thr-Ser at position 71). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from gluthamine at position 23.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA334609) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10785> (SEQ ID NOS: 40, 50, and 60)

Determination of the whole base sequence of the cDNA insert of clone HP10785 obtained from cDNA library of human kidney revealed the structure consisting of a 171-bp 5'-untranslated region, a 930-bp ORF, and a 318-bp 3'-untranslated region. The ORF encodes a protein consisting of 309 amino acid residues and there existed six putative transmembrane domains. Figure 20 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro

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translation resulted in formation of a translation product of high molecular weight.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI822041) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03878> (SEQ ID NOS: 61, 71, and 81)

Determination of the whole base sequence of the cDNA insert of clone HP03878 obtained from cDNA library of human kidney revealed the structure consisting of a 77-bp 5'-untranslated region, a 1800-bp ORF, and a 139-bp 3'untranslated region. The ORF encodes a protein consisting of 599 amino acid residues and there existed ten putative Figure 21 depicts the transmembrane domains. hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to flounder (Pseudopleuronectes americanus) Na/Pi cotransport system protein (Accession No.

94

AAB16821). Table 12 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and flounder Na/Pi cotransport system protein (PN). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 57.1% in the region of 545 amino acid residues other than the N-terminal and C-terminal regions.

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Table 12

| * *. ***. *. * *  | *. **          |
|---|----------------|
| PN MAPRQKVGTNSSPKPALDDDAPVGNIPPAYSTLDLVSDDPDADPWNAPELIDNGVF | KWSEL          |
| HP RVAGRLRRVAGSVLKACGLLGSLYFFICSLDVLSSAFQLLGSKVAGDIFKDNVVLS | SNPVA          |
| . ***** .** ********************                            | ****           |
|   |                |
| PN DTKGKMMRVLTGLLKLVALLGLLYFFICSLDVLSSAFQLVGGKAAGDIFKDNAVL  | HINLAH         |
|   |                |
| HP GLVIGVLVTALVQSSSTSSSIVVSMVAAKLLTVRVSVPIIMGVNVGTSITSTLVS  | MAQSG          |
| ***************************************                     | <b>*</b> *. *  |
| PN GLVIGVLVTVMVQSSSTSSSIVVSMVSSGLLDVQSAVPIIMGANIGTSVTNTIVA  | MMQAG          |
|   |                |
| HP DRDEFQRAFSGSAVHGIFNWLTVLVLLPLESATALLERLSELALGAASLTPRAQA  | PDILK          |
| **. **. ***. * ** ***. **. **** ** *                        | <b>*</b> *. *. |
| PN DRNEFRRAFAGATVHDFFNWLAVLILLPLEVATGVLYKLTHLIIESFNIQGGEDA  | PDLLN          |
| ·   |                |
| HP VLTKPLTHLIVQLDSDMI—MSSATGNATNSSLIKHWCGTTGQPT——QENSSCG    | AFGPC          |
| *, *, ***, *****, * *, * ****, ** * * *                     | * . *          |
| PN VITDPLTDSIVQLDKNVISLIATNDEAAVNMSLIKEWCKTKTNVTFWNATVENCT  | AGALC          |
|   |                |
| HP TEKNSTAPADRLPCRHLFAGTELTDLAYGCILLAGSLLVLCGCLVLI          | VKLLN          |
| *   | ****           |
| PN WEEGNLTWTMLNKTWIINQERCKHIFANTTLPDLAYGLILLALSLFYLCTCLILI  | VKLLN          |

- HP SVLRGRVAQVVRTVINADFPFPLGWLGGYLAVLAGAGLTFALQSSSVFTAAVVPLMGVGV

  \*. \*. \*. \*\* \*. \*\*\*. \*\*\*\*\* \*. . \*\*\*. \*\* . \*\*\*. \*\* . \*\*\*
  PN SMLKGQVAVVIKRVINTDFPFPFCWVTGYIAIFVGAGMTFIVQSSSVFTSAITPLVGIGV
- HP ISLDRAYPLLLGSNIGTTTTALLAALASPADRMLSALQVALIHFFFNLAGILLWYLVPAL
- PN ISLERAYPLTLGSNIGTTTTAILAAMASPAEKLKESLQIALCHFFFNVMGILLFYPIPFT

- PN RVP I RLARGLGNHTAKYRWFAGLYLVLCFLVFPLTVFGLSMAGWQVLVGVGVPFVVL I VF
- HP VILVTVLQRRRPAWLPVRLRSWAWLPVWLHSLEPWDRLVTRCCPCNVCSPPKATTKEAYC
- PN VIVVNVMQSRCPRFLPKVLQDWDFLPRPLHSMAPWDTVVTSALGFCGKYCCCCKCCKKT
- HP YENPEILASQQL
- PN EDENMKNNTKSLEMYDNPSMLKDEDTKEASKATHL

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI792826) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

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<HP03884> (SEQ ID NOS: 62, 72, and 82)

Determination of the whole base sequence of the cDNA insert of clone HP03884 obtained from cDNA library of human kidney revealed the structure consisting of a 336-bp 5'-untranslated region, a 246-bp ORF, and a 864-bp 3'untranslated region. The ORF encodes a protein consisting of 81 amino acid residues and there existed one putative Figure 22 depicts the domain. transmembrane hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 10 kDa that was almost identical with the molecular weight of 8,928 predicted from the ORF.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to rat cortexin (Accession No. P41237). Table 13 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and rat

cortexin (RC). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 47.9% in the entire region.

Table 13

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- - RC MSAPWTLSPEPLPPSTGPPVGAGLDVEQRTVFAFVLCLLVVLVLLMVRCVRILLDPYSRM
- RC PASSWTDHKEALERGQFDYALV

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI791379) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03934> (SEQ ID NOS: 63, 73, and 83)

25 Determination of the whole base sequence of the

cDNA insert of clone HP03934 obtained from cDNA library of human kidney revealed the structure consisting of a 39-bp 5'-untranslated region, a 1965-bp ORF, and a 463-bp 3'-untranslated region. The ORF encodes a protein consisting of 654 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 23 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 80 kDa that was larger than the molecular weight of 74,110 predicted from the ORF. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from arginine at position 28.

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The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human  $\beta$ -galactosidase (Accession No. AAC12775). Table 14 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and human  $\beta$ -galactosidase (BG). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 54.6% in the entire region.

Table 14

| Die 14   |   |
|--|---|
| MAPKKLSCLRSLLLPLSLTLLLPQADTRSFVVDRGHDRFLLDGAPFRYVSGSLHY        |   |
| MPGFLVRILLLLVLLLLGPTRGLRNATQRMFEIDYSRDSFLKDGQPFRYISGSIHY       |   |
| FRVPRVLWADRLLKMRWSGLNAIQFYVPWNYHEPQPGVYNFNGSRDLIAFLNEAALANLI   |   |
| **** * ****** ****** *****. *** ** *. *.                       |   |
| P VILRPGPYICAEWEMGGLPSWLLRKPEIHLRTSDPDFLAAVDSWFKVLLPKIYPWLYHN  |   |
| ***** <u>*</u> ******************                              | ŧ |
| G VILRPGPYICAEWEMGGLPAWLLEKESILLRSSDPDYLAAVDKWLGVLLPKMKPLLYQN  | Ĵ |
| P GNIISIQVENEYGSYRACDFSYMRHLAGLFRALLGEKILLFTTDGPE—GLKCGSLRGL   |   |
| * .******* **** **** *. ** ** ******                           | * |
| G GPVITVQVENEYGSYFACDFDYLRFLQKRFRHHLGDDVVLFTTDGAHKTFLKCGALQGL  | Y |
| IP TTVDFGPADNMTKIFTLLRKYEPHGPLVNSEYYTGWLDYWGQNHSTRSVSAVTKGLENM | L |
| *******. *.   *   **. **. ***. ****. *** ***                   | ‡ |
| BG TTVDFGTGSNITDAFLSQRKCEPKGPLINSEFYTGWLDHWGQPHSTIKTEAVASSLYDI | L |
| HP KLGASVNMYMFHGGTNFGYWNGADKKGRFLPITTSYDYDAPISEAGDPTPKLFALRDVI | S |
| *****. *** *****. ***** *******                                | ř |
|  |   |

BG ARGASVNLYMFIGGTNFAYWNGAN—SPYAAQPTSYDYDAPLSEAGDLTEKYFALRNIIQ

| HP | KFQEVPLGPLPPPSPKMMLGPVTLHLVGHLLAFLDLLCPRGPIHSILPMTFEAVKQDHGF   |
|----|--|
|    | **** **.****.  |
| BG | KFEKVPEGPIPPSTPKFAYGKVTLEKLKTVGAALDILCPSGPIKSLYPLTFIQVKQHYGF   |
| HP | MLYRTYMTHTIFEPTPFWVPNNGVHDRAYYMVDGVFQGVVERNMRDKLFLTGKLGSKLDI   |
|    | . * * * *  |
| BG | VLYRTTLPQDCSNPAPLSSPLNGVHDRAYVAVDGIPQGVLERNNVITLNITGKAGATLDL   |
|    |  |
| НP | LVENMGRLSFGSNSSDFKGLLKPPILGQTILTQWMMFPLKIDNLVKWW-FPLQ          |
|    | ********* ****** * ***. *                                      |
| BG | LVENMGRVNYGAYINDFKGLVSNLTLSSNILTDWTIFPLDTEDAVRSHLGGWGHRDSGHH   |
| HP | LPKWPYPQAP-SGPTFYSKTFPILGSVGDTFLYLPGWTKGQVWINGFNLGRYWTKQ       |
|    | * *.** .*. * *****************                                 |
| BG | DEAWAHNSSNYTLPAFYMGNFSIPSGIPDLPQDTFIQFPGWTKGQVWINGFNLGRYWPAR   |
| HP | GPQQTLYVPRFLLFPRGALNKITLLELE——DVPLQPQVQFLDKPILNSTSTLHRTH       |
|    | *** **. ** * *. **. ***  |
| BG | G GPQLTLFVPQHILMTSAP-NTITVLELEWAPCSSDDPELCAVTFVDRPVIGSSVTYDHPS |
| HI | PINSLSADTLSASEPMELSGH  |
|    |  |

BG KPVEKRLMPPPPQKNKDSWLDHV

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PCT/JP00/09359

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI907720) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03949> (SEQ ID NOS: 64, 74, and 84)

Determination of the whole base sequence of the cDNA insert of clone HP03949 obtained from cDNA library of 👵 human kidney revealed the structure consisting of a 244-bp 5'-untranslated region, a 1173-bp ORF, and a 33-bp 3'untranslated region. The ORF encodes a protein consisting of 390 amino acid residues and there existed ten putative transmembrane domains. Figure 24 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human solute carrier family 16 (Accession No. NM\_004696). Table 15 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and human solute carrier family 16

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(HS). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 98.7% in the region other than the N-terminal and C-terminal regions.

| Table | 15   |
|-------|--|
| HP    | MGMDDCDSFFPGPLVAIICDILGEKTTSILGAFVVTGGYLISSWATSIPFLCVTMGLL           |
|       | * . ***********************************                              |
| HS    | WIGSIMSSLRFCAGPLVAIICDILGEKTTSILGAFVVTGGYLISSWATSIPFLCVTMGLL         |
|       |  |
| HP    | PGLGSAFLYQVAAVVTTKYFKKRLALSTAIARSGMGLTFLLAPFTKFLIDLYDWTGALIL         |
|       | ***************************************                              |
| HS    | PGLGSAFLYQVAAVVTTKYFKKRLALSTAIARSGMGLTFLLAPFTKFLIDLYDWTGALIL         |
|       |  |
| HP    | FGAIALNLVPSSMLLRPIHIKSENNSGIKDKGSSLSAHGPEAHATETHCHETEESTIKDS         |
| •     | ***************************************                              |
| ·HS   | ${\tt FGAIALNLVPSSMLLRPIHIKSENNSGIKDKGSSLSAHGPEAHATETHCHETEESTIKDS}$ |
| ٠     |  |
| HP    | TTQKAGLPSKNLTVSQNQSEEFYNGPNRNRLLLKSDEESDKVISWSCKQLFDISLFRNPF         |
|       | ***************************************                              |
| HS    | TTQKAGLPSKNLTVSQNQSEEFYNGPNRNRLLLKSDEESDKVISWSCKQLFDISLFRNPF         |
|       |  |
| HP    | FYIFTWSFLLSQLAYFIPTFHLVARAKTLGIDIMDASYLVSVAGILETVSQIISGWVADQ         |
|       | ***************************************                              |
| HS    | FYIFTWSFLLSQLAYFIPTFHLVARAKTLGIDIMDASYLVSVAGILETVSQIISGWYADQ         |
| HP    | NWIKKYHYHKSYLILCGITNLLAPLATTFPLLMTYTICFAIFAGGYLALILPYLYDLCRN         |
|       | ***************************************                              |
| HS    | NWIKKYHYHKSYLILCGITNLLAPLATTFPLLMTYTICFAIFAGGYLALILPYLVDLCRN         |
|       |  |
| HP    | STVNRFLGLASFFAGMAVLSGPPIAGNTFTTF                                     |
|       | ******* .  |
| HS    | STVNRFLGLASFFAGMAVLSGPP I AGWLYDYTQTYNGSFYFSGICYLLSSVSFFFVPLAE       |

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AW239415) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

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<HP03959> (SEQ ID NOS: 65, 75, and 85)

Determination of the whole base sequence of the cDNA insert of clone HP03959 obtained from cDNA library of human kidney revealed the structure consisting of a 7-bp 5'untranslated region, a 1359-bp ORF, and a 531-bp 3'untranslated region. The ORF encodes a protein consisting of 452 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 25 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 53 kDa that was somewhat larger than the molecular weight of 50,798 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 55 kDa. In addition, there exists in the amino acid sequence of this protein three sites at which N-glycosylation may occur (Asn-Phe-Ser at position 64, Asn-Gly-Ser at position 126 and Asn-Val-Thr at position 362). Application of the (-3,-1) rule, a

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method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from alanine at position 27.

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The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to Arabidopsis thaliana putative carboxypeptidase (Accession No. AAD21510). Table 16 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and Arabidopsis thaliana putative carboxypeptidase (AC). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 44.3% in the region of 323 amino acid residues other than the N-terminal and C-terminal regions.

| Table | e 16   |
|-------|--|
| HP    | ${\tt MELALRRSPVPRWLLLLPLLLGLNAGAVIDWPTEEGKEVWDYVTVRKDAYMFWWLYYATM}$   |
|       |  |
| AC    | MDPKLGDTSKLDQHTCFGG I IKV  |
|       |  |
| HP    | ${\tt SCKNFSELPLVMWLQGGPGGSSTGFGNFEE}{\tt I}{\tt GPLDSDLKPRKTTWLQAASLLFVDNPVGTAASLTAASLTAASLLFVDNPVGTAASLTAASLTAASLTAASLTAASLTAASLTAASLTAAS$ |
|       | *. *.**.***.*. **** ****. *. ***   |
| AC    | HIELKILPSHGLSSSGSKGASGVGIGNFQEVGPLDTFLKPRNSTWLKKADLLFVDSPVGA   |
|       |  |
| HP    | GFSYVNGS-GAYAKDLAMVASDMMVLLKTFFSCHKEFQTVPFYIFSESYGGKMAAGIGI  |
|       | *. *. *. *.   .   . *. *.   . * *.   . *.   . * * . *  |
| . AC  | GYSFVEGNQKDLYVKSDEEAAQDLTKLLQQLFNKNQTLNQSPLFIVAESYGGKIAVKLGI   |
|       |  |
| HP    | ELYKA I QRGT I KCNF AGVALGDSW I SPVDSVLSWGPYLYSMSLLEDKGLAEVSKVAEQVL  |
|       | *. *. * * * * * * * * * *  |
| AC    | SVIDAVQSGKLKLHLGGVILGDSWISPEDFVFSWGPLLKHVSRLDDNGLDSSNSLAEKIK   |
|       |  |
| HP    | NAVNKGLYREATELWGKAEMI IEQNTDGVNFYN-ILTKSTPTSTMESSLEFTQSHLV   |
|       | * * . **. * . * . *. *. *. *. *  |
| AC    | TQIKNGEYVGATQTWMDLENLISSKSNFVDFYNFLLDTGMDPVSLTTSLKIKKEEKIKKY   |
|       |  |
| HP    | CLCQ-RHVRHLQRDALSQLMNGPIRKKLKIIPEDQSWGGQATNVFVNMEEDFMKPV   |
|       | . * . *  |
| AC    | SRYLNDMRSLSDVEDVEGDLDKLMNGVIKKKLKIIPNDLIWGNNSDDVFTAMEAAFMKPY   |
|       | ·  |
| HP    | ISIVDELLEAGINVTVYNGQLDLIVDTMGQEAWVRKLKWPELPKFSQLKWKALYSDPKSI   |
|       | *. ********.******.*.*.*   |
| AC    | IEDVDELLATGVDVTIYNGQLDVICSTSGTEAWVHKLR   |

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. T59065) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

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<HP03983> (SEQ ID NOS: 66, 76, and 86)

Determination of the whole base sequence of the cDNA insert of clone HP03983 obtained from cDNA library of human kidney revealed the structure consisting of a 42-bp 5'-untranslated region, a 1473-bp ORF, and a 341-bp 3'-untranslated region. The ORF encodes a protein consisting of 490 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain at the C-terminus. Figure 26 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glutamic acid at position 22.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human ClqR protein (Accession No. AAB53110). Table 17 shows the comparison between amino acid

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sequences of the human protein of the present invention (HP) and human ClqR protein (HC). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 25.8% in the N-terminal region of 310 amino acid residues. Since the positions of 17 cysteine residues are conserved, in particular, the two proteins are considered to assume similar higher-order structures.

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Table 17

| HP | MRPAFALCLLWQALWPGPGGGEHPTADRAGCSASGACYSLHHATMKRQAAEEACILRGG            |
|----|--|
|    | * * **   |
| HC | MATSMGLLLLLLLLTQPGAGTGADTEAVVC-VGTACYTAHSGKLSAAEAQNHCNQNGGI            |
| HP | LSTVRAGAELRAVLALLRAGPGPGGGSKDLLFWVALERRRSHCTLENEPLRGFSWLSS             |
|    | *. ** *  |
| HC | LATVKSKEEAQHVQRVLAQLLRREAALTARMSKFWIGLQREKGKCLDPSLPLKGFSWV-            |
| HP | DPGGLESDTLQWVEEPQRSCTARRC—AVLQATGGVEP—AGWKEMRC—HLRAN  ** * . * * * * * |
| HC | -GGGEDTPYSNWHKELRNSCISKRCVSLLLDLSQPLLPNRLPKWSEGPCGSPGSPGSNIE           |
| HP | GYLCKYQFEVLCPAPRPGAASNLSYRAPFQLHSAALDFSPPGTEVSALCRGQLP1S               |
|    | ***. * * * * * *   |
| HC | GFYCKFSFKGMCRPLALGGPGQVTYTTPFQTTSSSLEAVPFASAANVACGEGDKDETQSH           |
| HP | -VTCIADEIGA-RWDKLSGDVLCPCPGRYLRAGKCAELPNCLD-DLGGFACECATGFE             |
|    | * *. *. **. * * * * *. * * *. *  |
| HC | YFLCKEKAPDVFDWGSSGPLCVSPKYGCNFNNGGCHQDCFEGGDGSFLCGCRPGFR               |

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- HP LGKDGRSCVTSGEGQPTLGGTGVPTRRPPATATSPVPQRTWPIRVDEKLGETPLVPEQDN

  \* . \* . \*.
  - ${\tt HC-LLDDLVTCASRNPCSSSPCRGGATCVLGPHGKNYTCRCPQGYQLDSSQLDCVDVDECQDS}$
  - HP SVTSIPEIPRWGSQSTMSTLQMSLQAESKATITPSGSVISKFNSTTSSATPQAFDSSSAV
  - HC PCAQECVNTPGGFRCECWVGYEPGGPGEGACQDVDECALGRSPCAQGCTNTDGSFHCSCE
  - ${\tt HP} \quad {\tt VFIFVSTAVVVLVILTMTVLGLVKLCFHESPSSQPRKESMGPPGLESDPEPAALGSSSAH}$
  - HC EGYVLAGEDGTQCQDVDECVGPGGPLCDSLCFNTQGSFHCGCLPGWVLAPNGVSCTMGPV
  - HP CTNNGVKVGDCDLRDRAEGALLAESPLGSSDA
  - HC SLGPPSGPPDEEDKGEKEGSTVPRAATASPTRGPEGTPKATPTTSRPSLSSDAPITSAPL

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. R51653) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10745> (SEQ ID NOS: 67, 77, and 87)

Determination of the whole base sequence of the cDNA insert of clone HP10745 obtained from cDNA library of human umbilical cord blood revealed the structure consisting of a 261-bp 5'-untranslated region, a 1179-bp ORF, and a 733-bp 3'-untranslated region. The ORF encodes a protein consisting of 392 amino acid residues and there existed nine putative transmembrane domains. Figure 27 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. R59881) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

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Determination of the whole base sequence of the cDNA insert of clone HP10775 obtained from cDNA library of human kidney revealed the structure consisting of a 30-bp 5'-untranslated region, a 1617-bp ORF, and a 287-bp 3'untranslated region. The ORF encodes a protein consisting of 538 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 28 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 66 kDa that was larger than the molecular weight of 55,133 predicted from the ORF. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from serine at position 23.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA366320) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10782> (SEQ ID NOS: 69, 79, and 89)

Determination of the whole base sequence of the cDNA insert of clone HP10782 obtained from cDNA library of 25

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human kidney revealed the structure consisting of a 70-bp 5'-untranslated region, a 309-bp ORF, and a 1501-bp 3'-untranslated region. The ORF encodes a protein consisting of 102 amino acid residues and there existed three putative transmembrane domains. Figure 29 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein.

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI815463) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10787> (SEQ ID NOS: 70, 80, and 90)

Determination of the whole base sequence of the cDNA insert of clone HP10787 obtained from cDNA library of human kidney revealed the structure consisting of a 54-bp 5'-untranslated region, a 1329-bp ORF, and a 912-bp 3'-untranslated region. The ORF encodes a protein consisting of 442 amino acid residues and there existed one putative transmembrane domain at the N-terminus. Figure 30 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product

of 50 kDa that was almost identical with the molecular weight of 50,562 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 56 kDa. In addition, there exists in the amino acid sequence of this protein four sites at which N-glycosylation may occur (Asn-Leu-Thr at position 83, Asn-Phe-Thr at position 89, Asn-Ala-Ser at position 113 and Asn-Lys-Ser at position 151).

acid sequence of the present protein revealed that the protein was similar to rat PV-1 (Accession No. AAD41524).

Table 18 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and rat PV-1 (RP). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 61.1% in the entire region.

| Tab | ole 18   |
|-----|--|
| HP  | MGLAMEHGGSYARAGGSSRGCWYYLRYFFLFVSLIQFLIILGLVLFMVYGNVHVSTESNL |
|     | ***. * *. *. *. *. ****************                          |
| RP  | MGLSMDR-SPYSRTGDRDRGCWYYLRYFFLFVSLIQFLIILGLVLFMIYGNVHATTESSL |
|     |  |
| HP  | QATERRAEGLYSQLLGLTASQSNLTKELNFTTRAKDAIMQMWLNARRDLDRINASFRQCQ |
|     | . *** ** **** **. *. *. **. * . ** * . ** * . ** * * ******  |
| RP  | RATEIRADNLYSQVVGLSAAQANLSKQLNISTLVKDTVMQQLLTTRREVERINASFRQCQ |
|     |  |
| HP  | GDRVIYTNNQRYMAAIILSEKQCRDQFKDMNKSCDALLFMLNQKVKTLEVEIAKEKTICT |
|     | ** . * . * . * . ********** . * . * . *                      |
| חמ  | GDLITYINYNRFIAAIILSEKQCQEQLKEGNKTCEALLFKLGEKVKTLEMEVVKEKAVCS |
| RP. | GDF1111M14KL14411F2EV606F6FVFGWF1CFVFFFVFCFWF1AFFWF1AFFWF1A  |
|     |  |
| HP  | KDKESYLLNKRVAEEQLVECYKTRELQHQERQLAKEQLQKVQALCLPLDKDKFEMDLRNL |
|     | ***, *, * . ** ** * . * *. ** *. * ***, ***, *******. **.    |
| RP  | KDKDSLLAGKRQAEMQQEACGKAREQQKQDQQVTEEQLRKVQSLCLPLDQEKFQADVLNV |
|     |  |
| HP  | WRDSIIPRSLDNLGYNLYHPLGSELASIRRACDHMPSLMSSKVEELARSLRADIERVARE |
|     | ****. *****. * . * . * . * . * . * . *                       |
| RP  | WRDSLVYRSLDNIGYH-Y-SLMPEFSSLRRTCESLPGIMTTKVEELARGLRAGIERVTRE |
|     |  |
| HP  | NSDLQRQKLEAQQGLRASQEAKQKVEKEAQAREAKLQAECSRQTQLALEEKAVLRKERDN |
|     | **.***** ** *******  |
| RP  |  |
| -14 |  |
| HP  | LAKELEEKKREAEQLRMELAIRNSALDTCIKTKSQPMMPVSRPMGPVPNPQPIDPASLEE |
| 111 | * ** *** **** * * ******* * * ** *                           |
|     |  |
| RP  | LERQLEARKRELEQLRTEVDVRISALDTCVKAKSLPAIQ-PRLPGPPPNPPPIDPASLEE |

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## HP FKRKILESQRPPAGIPVAPSSG

\*\*. \*\*\*\*\*\*\* \*. . \*. \*\*

## RP FKKRILESQRPPLVNPAVPPSG

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AL041217) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03977> (SEQ ID NOS: 91, 101, and 111)

Determination of the whole base sequence of the CDNA insert of clone HP03977 obtained from cDNA library of human kidney revealed the structure consisting of a 35-bp 5'-untranslated region, a 684-bp ORF, and a 1175-bp 3'-untranslated region. The ORF encodes a protein consisting of 227 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain at the C-terminus. Figure 31 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 29 kDa that was larger than the molecular weight of 25,926 predicted from the ORF. Application of the (-3,-1)

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rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from leucine at position 30.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human gp25L2 (Accession No. CAA62380). Table 19 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and human gp25L2 (GP). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 78.5% in the region other than the N-terminal region.

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Table 19 .

| HP | MAGYGAGPLRAMGRQALLLLALCATGAQGLYFHIGETEKRCFIEEIPDETMVIGNYRTQM |
|----|--|
|    | * **, * * . * **********************                         |
| GP | MRTLLLVLWLATRGS-ALYFHIGETEKKCFIEEIPDETMVIGNYRTQL             |
| HP | WDKQKEVFLPSTPGLGMHVEVKDPDGKVVLSRQYGSEGRFTFTSHTPGDHQICLHSNSTR |
|    | . ***. * . *. *** ** ****** . **. *. *.                      |
| GP | YDKQREEYQPATPGFGMCVEVKDPEDKVILAREYGSEGRFTFTSHTPGEHQICLHSNSTK |
| HP | MALFAGGKLRYHLDIQVGEHANNYPEIAAKDKLTELQLRARQLLDQVEQIQKEQDYQRYR |
|    | ******. **************. * *****. ****. *** ******            |
| GP | FSLFAGGMLRVHLDIQVGEHANDYAEIPAKDKLSELQLRVRQLVEQVEQIQKEQNYQRWR |
| HP | EERFRLTSESTNQRVLWWS1AQTV1L1LTG1WQMRHLKSFFEAKKLV              |
|    | ***** ********* **. ***. **********                          |
| GP | EERFRQTSESTNQRVLWWSILQTLILVAIGVWQMRHLKSFFEAKKLV              |

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AR052481, U.S. Patent No. 5831052) in patent data. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

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<HP10649> (SEQ ID NOS: 92, 102, and 112)

Determination of the whole base sequence of the cDNA insert of clone HP10649 obtained from cDNA library of the human epidermoid carcinoma cell line KB revealed the structure consisting of a 114-bp 5'-untranslated region, a 1059-bp ORF, and a 1240-bp 3'-untranslated region. The ORF encodes a protein consisting of 352 amino acid residues and there existed one putative transmembrane domain. Figure 32 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 40 kDa that was almost identical with the molecular weight of 39,774 predicted from the ORF.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to Epiphyas postvittana nucleopolyhedrovirus apoptosis inhibitor iap-1 (Accession No. AAD19698). Table 20 shows the comparison between amino

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acid sequences of the human protein of the present invention (HP) and Epiphyas postvittana nucleopolyhedrovirus apoptosis inhibitor iap-1 (EP). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 40.8% in the C-terminal region of 49 amino acid residues.

Table 20

HP MESGGRPSLCQFILLGTTSVVTAALYSVYRQKARVSQELKGAKKVHLGEDLKSILSEAPG HP KCVPYAVIEGAVRSVKETLNSQFVENCKGVIQRLTLQEHKMVWNRTTHLWNDCSKIIHQR MSATSPLY I INVCENAHEVSAEHVFNVL I ERHNSFENYP I DNVAFVNSL I INGF EP HP TNTVPFDLVPHEDGVDVAVRVLKPLDSVDLGLETVYEKFHPSIQSFTDVIGHYISGERPK EP RYQNYDDAVMCEYCSAVIKNWHEDDCVEFVHATLSPYCYYANKIAQNENFANNLSTNAFL HP GIQETEEMLKVGATLTGVGELVLDNNSVRLQPPKQGMQYYLSSQDFDSLLQRQESSVKLW EP VTPGKPICVYSRLTHTNARKSTFEDYWPAALQHLVANISEAGMFHTKLGDETACFFCDCR HP KYLALYFGFATCATLFFILRKQYLQRQERLRLKQMQEEFQEHEAQLLSRAKPEDRESLKS EP VRDWLPNDDPWQRHAIANPQCYFVVCIKGDEFCNAVRQRDELAPLQSVVALEHVSNDENM HP ACVVCLSSFKSCVFLECGHVCSCTECYRALPEPKKCPICRQAITRVIPLYNS \* , \*\*. . . \*, \* \* \* \* . \*\* \*\* . \*\*\*. \* . . . EP ECKICLERQRDTVLLPCRHFCVCMQCYFAL-DNKCPTCRQDVTDFVKIFVV

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. T50032) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

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<HP10779> (SEQ ID NOS: 93, 103, and 113)

Determination of the whole base sequence of the cDNA insert of clone HP10779 obtained from cDNA library of human kidney revealed the structure consisting of a 34-bp 5'-untranslated region, a 393-bp ORF, and a 1949-bp 3'-untranslated region. The ORF encodes a protein consisting of 130 amino acid residues and there existed two putative transmembrane domains. Figure 33 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AL042495) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention. In addition, this gene was mapped on chromosome 9q34 (Accession No. AC001644).

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<HP10790> (SEQ ID NOS: 94, 104, and 114)

Determination of the whole base sequence of the cDNA insert of clone HP10790 obtained from cDNA library of human kidney revealed the structure consisting of a 109-bp 5'-untranslated region, a 993-bp ORF, and a 53-bp 3'untranslated region. The ORF encodes a protein consisting of 330 amino acid residues and there existed one putative transmembrane domain. Figure 34 depicts hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 34 kDa that was smaller than the molecular weight of 36,642 predicted from the ORF.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AW241940) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10793> (SEQ ID NOS: 95, 105, and 115)

Determination of the whole base sequence of the cDNA insert of clone HP10793 obtained from cDNA library of human kidney revealed the structure consisting of a 70-bp 5'-untranslated region, a 1053-bp ORF, and a 206-bp 3'-

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untranslated region. The ORF encodes a protein consisting of 350 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain in the inner portion. Figure 35 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 40 kDa that was somewhat larger than the molecular weight of 37,134 predicted from the ORF. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glycine at position 25.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA326569) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10794> (SEQ ID NOS: 96, 106, and 116)

Determination of the whole base sequence of the cDNA insert of clone HP10794 obtained from cDNA library of human kidney revealed the structure consisting of a 146-bp 5'-untranslated region, a 342-bp ORF, and a 899-bp 3'-untranslated region. The ORF encodes a protein consisting of

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113 amino acid residues and there existed one putative transmembrane domain. Figure 36 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 14 kDa that was almost identical with the molecular weight of 12,017 predicted from the ORF.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, accession No. AI346561) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10797> (SEQ ID NOS: 97, 107, and 117)

Determination of the whole base sequence of the cDNA insert of clone HP10797 obtained from cDNA library of human kidney revealed the structure consisting of a 129-bp 5'-untranslated region, a 570-bp ORF, and a 459-bp 3'-untranslated region. The ORF encodes a protein consisting of 189 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 37 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product

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of 22 kDa that was almost identical with the molecular weight of 21,053 predicted from the ORF. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glutamine at position 23.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA356938) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention. In addition, this gene was mapped on chromosome 4 (Accession No. AC004067).

<HP10798> (SEQ ID NOS: 98, 108, and 118)

Determination of the whole base sequence of the cDNA insert of clone HP10798 obtained from cDNA library of human kidney revealed the structure consisting of a 25-bp 5'-untranslated region, a 834-bp ORF, and a 247-bp 3'untranslated region. The ORF encodes a protein consisting of 277 amino acid residues and there existed seven putative domains. Figure 38 depicts the transmembrane hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 27 kDa that was smaller than the molecular weight of

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30,685 predicted from the ORF.

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H92084) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10800> (SEQ ID NOS: 99, 109, and 119)

10 Determination of the whole base sequence of the cDNA insert of clone HP10800 obtained from cDNA library of human kidney revealed the structure consisting of a 158-bp 5'-untranslated region, a 825-bp ORF, and a 924-bp 3'untranslated region. The ORF encodes a protein consisting of 274 amino acid residues and there existed one putative 15 transmembrane domain. Figure 39 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product 20 of 33 kDa that was somewhat larger than the molecular weight of 31,108 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 45 kDa. In addition, there exists in the amino acid sequence of this protein five sites at which N-glycosylation may occur (Asn-25 Ile-Thr at position 145, Asn-Ile-Thr at position 151, Asn-

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Ile-Thr at position 164, Asn-Ile-Thr at position 183, and Asn-Thr-Thr at position 256).

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA729308) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

10 <HP10801> (SEQ ID NOS: 100, 110, and 120)

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Determination of the whole base sequence of the CDNA insert of clone HP10801 obtained from cDNA library of human kidney revealed the structure consisting of a 133-bp 5'-untranslated region, a 1173-bp ORF, and a 510-bp 3'-untranslated region. The ORF encodes a protein consisting of 390 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain in the inner portion. Figure 40 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation with the addition of microsome resulted in formation of a product of 50 kDa that was larger than the molecular weight of 41,097 predicted from the ORF. In addition, there exists in the amino acid sequence of this protein five sites at which N-glycosylation may occur (Asn-

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Leu-Ser at position 108, Asn-Val-Thr at position 169, Asn-Leu-Ser at position 213, Asn-Val-Thr at position 236 and Asn-Gly-Thr at position 307). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glutamine at position 30.

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The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human A33 antigen (Accession No. NP\_005805). Table 21 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and human A33 antigen (HA). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 28.7% in the intermediate region of 265 amino acod residues.

Table 21

| НР | MISLPGPLYTNLLRFLFLGLSALAPPSRAQLQLHLPANRLQAVEGGEVVLPAWY-TLHGE     |
|----|--|
| HA | MVGKMWPVLWTLCAVRVTVDAISVETPQDVLRASQGKSVTLPCTYHTSTSS              |
| HP | VSSSQPWEVPFVMWFFKQKEKEDQVLSYINGVTTSKPGVSLVYSMPSRNLSLRLEGLQEK     |
| HA | **  REGLIQWDKLLLTHTERVVIWPFSNKNYIHG-ELYKNRVSISNNAEQSDASITIDQLTMA |
| HP | DSGPYSCSVNVQDKQGKSRGHSIKTLELNVLVPPAPPSCRLQGVPHVGANVTLSCQSPRS     |
| НА | *. *. *. ***   |
| HP | KPAVQYQWDRQLPSFQTFFAPALDVIRGSLSLTNLSSSMAGVYVCKAHNEVGTAQCNVTL     |
| НА | . *. ** *. * * * * * * * * * * * * * * *                         |
| •  | EV-STGPGAAVVAGAVVGTLVGLGLLAGLVLLYHCRGKALEEPANDIKEDAIAPRTLPWP     |
|    | . * * * * *  |
| НР | KSSDTISKNGTLSSVTSARALRPPHGPPRPGALTPTPSLSSQALPSPRLPTTDGAHPQPI     |
| HA | PPEQLRELSREREEEDDYRQEEQRSTGRESPDHLDQ                             |

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. R33685) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03696> (SEQ ID NOS: 121, 131, and 141)

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Determination of the whole base sequence of the cDNA insert of clone HP03696 obtained from cDNA library of thuman umbilical cord blood revealed the structure consisting of a 184-bp 5'-untranslated region, a 1188-bp ORF, and a 589-bp 3'-untranslated region. The ORF encodes a protein consisting of 395 amino acid residues and there existed one putative transmembrane domain. Figure 41 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to rat cell surface glycoprotein GP42 (Accession No. P23505). Table 22 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and rat cell surface glycoprotein GP42 (RC). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of

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the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 46.1% in the intermediate region of amino acid residues 62-280.

Table 22

| HP | ${\tt MSGMEEYTTVSGEVLQRWKIPSFKENQTLSMGAATVQSRGQYSCSGQVMYIPQTFTQTSHEART SIGNATURE of the content o$ |
|----|--|
|    |  |
| RC | WLLWMATITO   |

- RC VSMTEAQELFQDPYLSRLNSSETSD---LLLKCTTKVDPNKPASELFYSFYKDNHIIQNR
- RC SHNPLFFISEANEENSGLYQCVVDAKDGTIQKKSDYLDIDLCTSVSQPVLTLQHEATNLA
- RC EGDKVKPLCETQLGSLP1LYSFYMDGE1LGEPLAPSGRAASLL1SVKAEWSGKNYSCQAE
- HP NSVSRERSEPKKLSLKGSQVLFTPASNWLVPWLPAS-LLGLMVIAAALLVYVRSWRKAGP

  \*. \*\*\*. \*\*\*\*. \* \* . . . . . \* \*\*\*. \* . . .
- RC NKVSRDISEPKKFPLVVSGTASMKSTT-VVIWLPVSCLVGWPWLLRF

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA446524) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03882> (SEQ ID NOS: 122, 132, and 142)

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Determination of the whole base sequence of the cDNA insert of clone HP03882 obtained from cDNA library of human kidney revealed the structure consisting of a 57-bp 5'-untranslated region, a 1653-bp ORF, and a 484-bp 3'untranslated region. The ORF encodes a protein consisting of 550 amino acid residues and there existed ten putative transmembrane domains. Figure 42 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to mouse solute carrier family 22 (cation transporter)-like protein (Accession No. NP\_033229). Table 23 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and mouse

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solute carrier family 22 (cation transporter)-like protein (MS). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 48.9% in the entire region.

| Tak | ole 23   |
|-----|--|
| ΗР  | MAFSKLLEQAGGYGLFQTLQVLTFILPCLMIPSQMLLENFSAAIPGHRCWTHMLDNG                  |
|     | ******* ** .* * * *******  |
| MS  | MAFPELLDRYGGLGRFQLFQTVALVTPILWVTTQNMLENFSAAVPHHRCWVPLLDNSTSQ               |
|     | SAVSTNMTPKALLTISIPPGPNQGPHQCRRFRQPQWQLLDPNATATSWSEADTEPCVDGW               |
|     |  |
| MS  | ASIPGDLGPDVLLAVSIPPGPDQQPHQCLRFRQPQWQLTESNATATWWSDAATEPCEDGW               |
| HP  | ${\tt VYDRSVFTSTIVAKWDLVCSSQGLKPLSQSIFMSGILVGSFIWGLLSYRFGRKPMLSWCC}$       |
|     | ***. *. * **** *****. **. * ***** * * **** * . * . * * * *                 |
| MS  | VYDHSTFRSTIVTTWDLVCNSQALRPMAQSIFLAGILVGAAVCGHASDRFGRRRVLTWSY               |
| מנו | LQLAVAGTSTIFAPTFVIYCGLRFVAAFGMAGIFLSSLTLMVEWTTTSRRAVTMTVVGCA               |
| ш   | * * . * * * * . * . *  |
| MS  | LLVSVSGTAAAFMPTFPLYCLFRFLLASAVAGVMMNTASLLMEWTSAQGSPLVMTLNALG               |
| HP  | FSAGQAALGGLAFALRDWRTLQLAASVPFFAISLISWWLPESARWLIIKGKPDQALQELR               |
|     | ** **.   |
| MS  | FSFGQVLTGSVAYGVRSWRMLQLAVSAPFFLFFVYSWWLPESARWLITVGKLDQGLQELQ               |
| HP  | KVARINGHK-EAKNLTIEVLMSSVKEEVASAKEPRSVLDLFCVPVLRWRSCAMLVVNFSL               |
|     | . ** . * . * * **. ** * * * * * * * *                                      |
| MS  | RVAAVNRRKAEGDTLTMEVLRSAMEEEPSRDKAGASLGTLLHTPGLRHRTIISMLCWFAF               |
| ••• | A A A ANTON A DO A GODA TO A A A ECANDRI CDATTALLI CRI CRRTINACCOANACI A I |
| H   | LISYYGLVFDLQSLGRDIFLLQALFGAVDFLGRATTALLLSFLGRRTIQAGSQAMAGLAI               |
|     | ***. ***. **. ******* * *** **. * **** * ** *                              |
| 1/0 | crtevel aldioal centri i oal i givdfpyktgslll i srlgrrlcovsflylpglci       |

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HP LANMLVPQDLQTLRVVFAVLGKGCFGISLTCLTIYKAELFPTPVRMTADGILHTVGRLGA

\*. \*. \*\*\*.... \*\* ... \*\*\*. \*\*... \*\*\*... \*\*\*\*\* \*.... \*\*\*

MS LSNILVPHGMGVLRSALAVLGLGCLGGAFTCITIFSSELFPTVIRMTAVGLCQVAARGGA

HP GNRQEAVTVESTSL

. ... .. \*\*.\*

MS HDTPDGSILMSTRL

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI242210) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

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<HP03903> (SEQ ID NOS: 123, 133, and 143)

Determination of the whole base sequence of the cDNA insert of clone HP03903 obtained from cDNA library of human kidney revealed the structure consisting of a 108-bp 5'-untranslated region, a 657-bp ORF, and a 1988-bp 3'-untranslated region. The ORF encodes a protein consisting of 218 amino acid residues and there existed three putative

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transmembrane domains. Figure 43 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 26 kDa that was somewhat larger than the molecular weight of 23,487 predicted from the ORF.

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The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to mouse prominin (Accession No. NP\_032961). Table 24 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and mouse prominin (MP). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 27.6% in the region other than the N-terminal and C-terminal regions.

| Tal | ole 24  |
|-----|---|
| ΗР  | MKHTLALLAPLLGLGLGLALSQLAAGATDCKFLGPAEHLTFTPAARARWLAPRVRAPGLL  |
|     | .* * *.* *  |
| MP  | MALYFSALLLLGLCGKISSEGQPAFHNTPGAMNYELPT-TKYETQDTFNAGIV   |
|     |   |
| HP  | DSLYGTVRRFLSVVQLNPFPSELVKALLNELA-SVKVNEVVRYEAGYVVCAVIAGLYL  |
|     | ** *. **. *** * ** . *. * *   |
| MP  | GPLYKMYHIFLNYVQPNDFPLDLIKKLIQNKNFDISVDSKEIALYEIGVLICAILGLLFI  |
|     |   |
| HP  | ${\tt LLVPTAGLCFCCCRCHRRCGGRVKTEHK-ALACERAALMVFLLLTTLLLLIGVVCAFVTN}$  |
|     | .*.*.* ** *** *** |
| МP  | ${\tt ILMPLYGCFFCMCRCCNKCGGEMHQRQKQNAPCRRKCLGLSLLYICLLMSLGIIYGFVAN}$  |
|     |   |
| HP  | QRTHEQMGPSIEAMPETLLSLWGLVSDVPQVSTVTPHPHVPL  |
|     | <b>*</b> . <b>* * *</b> .   |
| MP  | QQTRTRIKGTQKLAKSNFRDFQTLLTETPKQIDYVVEQYTNTKNKAFSDLDGIGSVLGGR  |

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI792608) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03974> (SEQ ID NOS: 124, 134, and 144)

Determination of the whole base sequence of the cDNA insert of clone HP03974 obtained from cDNA library of human kidney revealed the structure consisting of a 41-bp 5'-untranslated region, a 1791-bp ORF, and a 253-bp 3'untranslated region. The ORF encodes a protein consisting of 596 amino acid residues and there existed twelve putative domains. 44 transmembrane Figure depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to rabbit (Oryctolagus cuniculus) sodium/glucose cotransporter protein (Accession No. AAA66065). Table 25 shows the comparison between amino acid sequences of the human protein of the present invention (HP)

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and rabbit sodium/glucose cotransporter protein (OC). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 89.1% in the entire region.

Table 25

| HP | M-AANSTSDLHTPGTQLSVADIIVITVYFALNVAVGIWSSCRASRNTVNGYFLAGRDMTW        |
|----|---|
|    | * *. ***** *. **. ***. **. ************                             |
| 00 | MVADNSTSDPHAPGPQLSVTDIVVITVYFALNVAVGIWSSCRASRNTVSGYFLAGRDMTW        |
|    |   |
| HP | WPIGASLFASSEGSGLFIGLAGSGAAGGLAVAGFEWNATYVLLALAWVFVPIYISSEIVT        |
|    | ******** . ***************** . ********                             |
| 00 | WPIGASLFGSSEGSGLFIGLAGSGAAGGLAVAGFDWNATYVLLALAWVFGAIYISSEIVT        |
|    |   |
| HP | LPEYIQKRYGGQRIRMYLSVLSLLLSVFTKISLDLYAGALFVHICLGWNFYLSTILTLGI        |
|    | *. ******. ****************************                             |
| OC | LAEYIQKRFGGQRIRMYLSVLSLLLSVFTKISLDLYAGALFVHICLGWNFYLSTILTLTI        |
| •  |   |
| HP | TALYTIAGGLAAVIYTDALQTLIMVVGAVILTIKAFDQIGGYGQLEAAYAQAIPSRTIAN        |
|    | ******. ***. ********************. ****. **. ****. *****. *****. ** |
| 00 | TALYTITGGLVAVIYTDALQTLIMVVGAVILAIKAFHQIDGYGQMEAAYARAIPSRTVAN        |

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| P   | TTCHLPRTDAMHMFRDPHTGDLPWIGNIFGLIIMAIWIWCIDQVIVQKSLSAKDLNHAKA   |
|-----|--|
|     | ******, ********, *********************  |
| DC. | TTCHLPRADAMHMFRDPYTGDLPWTGMTFGLTIMATWYWCTDQVIVQRSLSARNLNHAKA   |
|     |  |
| HP  | GSILASYLKMLPMGLIIMPGMISRALFPDDVGCVVPSECLRACGAEVGCSNIAYPKLVME   |
|     | ***************************************  |
| 0C  | GSILASYLKMLPMGLMIMPGMISRALFPDEVGCVVPSECLRACGAEIGCSNIAYPKLVME   |
|     |  |
| HP  | $LMP\ I\ GLRGLM\ I\ AVMLAALMSSLTS\ I\ FNSSSTLFTMD\ I\ WRRLRPRSGERELLL\ VGRLV\ I\ VARAMAR ARBOR ARBOR.$   |
|     | ***, **********, . ******, ************  |
| 0C  | LMPVGLRGLMIAVMMPALMSSLSSIFNSSSTLFTMDIWRRLRPCASERELLLVGRLVIVVILLVGRLVGRLVIVVILLVGRLVIVVILLVGRLVGRLVGRLVGRLVGRLVGRLVGRLVGRLVGRLVG   |
|     |  |
| HP  | $\verb Ligvsvawipvlqdsnsgqlfiymqsvtsslappvtavfvlgvfwrraneqgafwgliace                                      $  |
|     | **************************************   |
| 0C  | $\verb Ligvsyawipvlqgsnggqlfiymqsytsslappvtavftlgifwqraneqgafwgllamed and the statement of the$ |
|     |  |
| HP  | LVVGATRLVLEFLNPAPPCGEPDTRPAVLGSIHYLHFAVALFALSGAVVVAGSLLTPPPC   |
|     | *, ********* *, ******, . ******* ********   |
| 0C  | LAYGATRLVLEFLHPAPPCGAADTRPAVLSQLHYLHFAVALFVLTGAVAVGGSLLTPPP  |
|     |  |
| HP  | SVQIENLTWWTLAQDVPLGTKAGDGQTPQKHAFWARVCGFNAILLMCVNIFFYAYFA  |
|     | . ********** * **. ******** ******   |
| 0C  | RHQIENLTWWTLTRDLSLGAKAGDGQTPQRYTFWARVCGFNAILLMCVNIFFYAYFA  |
|     |  |

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI793336) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

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<HP03978> (SEQ ID NOS: 125, 135, and 145)

Determination of the whole base sequence of the cDNA insert of clone HP03978 obtained from cDNA library of human kidney revealed the structure consisting of a 99-bp 5'-untranslated region, a 1404-bp ORF, and a 705-bp 3'untranslated region. The ORF encodes a protein consisting of 467 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 45 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 55 kDa that was somewhat larger than the molecular weight of 52,352 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 57 kDa. In addition, there exists in the amino acid sequence of this protein two sites at which N-glycosylation may occur (Asn-Arg-Thr at position 78 and Asn-His-Ser at position 161). Application of the (-3,-1) rule, a method for predicting the

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cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from alanine at position 22.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human tubulo-interstitial nephritis antigen (Accession No. BAA84949). Table 26 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and human tubulo-interstitial nephritis antigen (TA). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 50.0% in the region other than the N-terminal region.

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|    | ble 26   |
|----|--|
| HP | MWRCPLGLLLLLPLAGHLALGAQQGRGRRELAPGLHLRGIRDAGGRYCQEQ  * **                  |
| TA | MWTGYKILIFSYLTTEIWMEKQYLSQREVDLEAYFTRNHTVLQGTRFKRAIFQGQYCRNF               |
| HP | DLCCRGRADDCALP-YLG-AICYCDLFCNRTVSDCCPDFWDFCLGVPPPFPPIQG                    |
|    | . ** . *. *. * . *. **** **. * . *** ** *                                  |
| TA | $\hbox{$\tt G-CCEDRDDGCVTEFYAANALCYCDKFCDRENSDCCPDYKSFCREEKEWPPHTQPWYPEG}$ |
| ΗР | CMHGGRIYPVLGTYWDNCNRCTCQENRQWQCDQEPCLVDPDMIKAINQGNYGWQAGNHSA               |
|    | **. *  |
| TA | CFKDGQHYEEGSVIKENCNSCTC-SGQQWKCSQHVCLVRPELIEQVNKGDYGWTAQNYSQ               |
| HP | FWGMTLDEGIRYRLGTIRPSSSVMNMHEIYTVLNPGEVLPTAFEASEKWPNLIHEPLDQG               |
|    | ******. * ****. ** * **. * ** *  |
| TA | FWGMTLEDGFKFRLGTLPPSLMLLSMNEMTASLPATTDLPEFFVASYKWPGWTHGPLDQK               |
| HP | NCAGSWAFSTAAVASDRVSIHSLGHMTPVLSPQNLLSCDTHQQQGCRGGRLDGAWWFLRR               |
| •  | ***. *******. **. ** *. *. ******. ** ** * . * ***. **.                    |
| TA | NCAASWAFSTASVAADRIAIQSKGRYTANLSPQNLISCCAKNRHGCNSGSIDRAWWYLRK               |
| HP | RGVVSDHCYPFSGRERDEAGPAPPCMMHSRAMGRGKRQATAHCPNSYVNNNDIYQVTPVY               |
|    | **. **. ***  |
| TA | RGLVSHACYPLF—KDQNATNNGCAMASRSDGRGKRHATKPCPNNVEKSNR I YQCSPPY               |
| HP | RLGSNDKEIMKELMENGPVQALMEVHEDFFLYKGGIYSHTPVSLGRPERYRRHGTHSVKI               |
|    | *********.*.******* **.***.*   |
|    |  |

TA RVSSNETEIMKEIMQNGPVQAIMQVHEDFFHYKTGIYRHVTSTNKESEKYRKLQTHAVKL

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HP TGWGEETLPDGRTLKYWTAANSWGPAWGERGHFRIVRGVNECDIESFVLGVWGRVGMEDM

\*\*\*\*. . . \*. \*. \*\*\*\*\*\* . \*\*\*. \*\*\*\*. . . \*

TA TGWGTLRGAQGQKEKFWIAANSWGKSWGENGYFRILRGVNESDIEKLIIAAWGQLTSSDE

HP GHH

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TA P

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. R48402) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10735> (SEQ ID NOS: 126, 136, and 146)

Determination of the whole base sequence of the cDNA insert of clone HP10735 obtained from cDNA library of human umbilical cord blood revealed the structure consisting of a 370-bp 5'-untranslated region, a 1431-bp ORF, and a 243-bp 3'-untranslated region. The ORF encodes a protein consisting of 476 amino acid residues and there existed ten putative transmembrane domains. Figure 46 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein.

The search of the protein database using the amino

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acid sequence of the present protein revealed that the protein was similar to Caenorhabditis elegans tetracycline resistance protein-like protein (Accession No. CAA94337).

Table 27 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and C. elegans tetracycline resistance protein-like protein (CP).

Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 51.5% in the intermediate region of 196 amino acid residues.

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| Ta | ble 27   |
|----|--|
| HP | MAGSDTAPFLSQADDPDDGPVPGTPGLPGSTGNPKSEEPEVPDQEGLQRITGLSPGRSAL       |
| CP | MVNSQQDYI  |
| HP | IVAVLCYINLLNYMDRFTVAGVLPDIEQFFNIGDSSSGLIQTVFISSYMVLAPVFGYLGD       |
|    | * * . *****. **. ****** **. ** . ******                            |
| CP | SYTALFYVNLLNYYDRYTVAGYLTQVQTYYNISDSLGGLIQTVFLISFMVFSPVCGYLGD       |
| HP | RYNRKYLMCGGIAFWSLVTLGSSFIPGEHFWLLLLTRGLVGVGEASYSTIAPTLIADLFV       |
|    | *. *** * * * *****. * ****. *.                                     |
| CP | RFNRKWIMIIGVGIWLGAVLGSSFVPANHFWLFLVLRSFVGIGEASYSNVAPSLISDMFN       |
| HP | ADQRSRMLSIFYFAIPVGSGLGYIAGSKVKDMAGDWHWALRYTPGLGVVAVLLLFLVVRE       |
|    | ** *********** *, **, * *, *, * * . *                              |
| CP | GQKRSTVFMIFYFAIPVGSGLGFIVGSNVATLTGHWQWGIRVSAIAGLIVMIALVLFTYE       |
| HP | PPRGAVERHSDLPPLNPTSWWADLRALARNLIFGLITCLTGVLGVGLGVEISRRLRHSNP * *** |
| CP | PERGAADKAMGESKDVVVTTNTTYLEDLVILLKTPTLVACTWGYTALVFVSGTLSWWEPT       |
| HP | RADPLVCATGLLGSAPFLFLSLACARGSIVATYIFIFIGETLLSMNWAIVADILLYVVIP       |
| CP | VIQHLTAWHQGLNDTKDLASTDKDRVALYFGAITTAGGLIGVIFGSMLSKWLVAGWGPFR       |
| HP | TRRSTAEAFQIVLSHLLGDAGSPYLIGLISDRLRRNWPPSFLSEFRALQFSLMLCAFVGA       |
| CP | RLQTDRAQPLYAGGGALLAAPFLLIGMIFGDKSLYLLYIMIFPGITPMCRNWGINIDMIT       |

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## HP LGGAAFLGTAIFIEADRRRAQLHVQGLLHEAGSTDDRIVVPQRGRSTRVPVASVLI

## CP TVIHPNRRSTAFSYFVLVSHLFGDASGPYLIGLISDAIRHGSTYPKDQYHSLVSATYCCV

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA460778) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention. Furthermore, the search has revealed the registration of sequences that shared a homology of 90% or more (Accession No. E12646) in patent data. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10750> (SEQ ID NOS: 127, 137, and 147)

Determination of the whole base sequence of the cDNA insert of clone HP10750 obtained from cDNA library of human umbilical cord blood revealed the structure consisting of a 262-bp 5'-untranslated region, a 1350-bp ORF, and a 564-bp 3'-untranslated region. The ORF encodes a protein consisting of 449 amino acid residues and there existed four putative transmembrane domains. Figure 47 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-

Doolittle method, of the present protein.

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AW304031) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10777> (SEQ ID NOS: 128, 138, and 148)

Determination of the whole base sequence of the cDNA insert of clone HP10777 obtained from cDNA library of human kidney revealed the structure consisting of a 15-bp 5'-untranslated region, a 318-bp ORF, and a 1030-bp 3'untranslated region. The ORF encodes a protein consisting of 105 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 48 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 14 kDa that was somewhat larger than the molecular weight of 11,603 predicted from the ORF. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glycine at position 30.

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Determination of the whole base sequence of the cDNA insert of clone HP10780 obtained from cDNA library of human kidney revealed the structure consisting of a 226-bp 5'-untranslated region, a 246-bp ORF, and a 571-bp 3'untranslated region. The ORF encodes a protein consisting of 81 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 49 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. translation resulted in formation of a translation product of 10 kDa that was somewhat larger than the molecular weight of 8,533 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 6 kDa. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glycine at position 25.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA658245) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

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Determination of the whole base sequence of the cDNA insert of clone HP10795 obtained from cDNA library of human kidney revealed the structure consisting of a 356-bp 5'-untranslated region, a 1659-bp ORF, and a 420-bp 3'untranslated region. The ORF encodes a protein consisting of 552 amino acid residues and there existed one transmembrane N-terminus. Figure 50 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. translation resulted in formation of a translation product of 65 kDa that was almost identical with the molecular weight of 64,280 predicted from the ORF.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human UDP-N-acetyl- $\alpha$ -Dgalactosamine:polypeptide N-acetylgalactosaminyltransferase 2 (Accession No. NP 004472). Table 28 shows the comparison between amino acid sequences of the human protein of the human UDP-N-acetyl-α-D-(HP) and invention galactosamine:polypeptide N-acetylgalactosaminyltransferase 2 (GA). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 49.9% in the entire region other than the N-terminal region.

| Tabl | .e 28   |
|------|---|
| HP   | MRRLTRRLVLPVFGVLWITVLLFFWVTKRKLEVPT   |
|      | **.   |
| GA   | MRRRSRMLLCFAFLWVLGIAYYMYSGGGSALAGGAGGGAGRKEDWNEIDPIKKKDLHHSN  |
| HP   | GPEVQTPKPSDADWDDLWDQFDERRYLNAKKWRVGDDPYKLYAFNQRESERISSNRAIPD  |
|      | * * * . * * * . *   |
| GA   | GEEKAQSMETLPPGKVRWPDFNQEAYVGGTMVRSGQDPYARNKFNQVESDKLRMDRAIPD  |
| HР   | TRHLRCTLLVYCTDLPPTSIIITFHNEARSTLLRTIRSVLNRTPTHLIREIILVDDFSND *** . * ***. ** ****. ****. *** ***. ***. ***. *** |
|      |   |
| GA   | TRHDQCQRKQWRVDLPATSVVITFHNEARSALLRTVVSVLKKSPPHLIKEIILVDDYSND  |
| НР   | PDDCKQLIKLPKVKCLRNNERQGLVRSRIRGADIAQGTTLTFLDSHCEVNRDWLQPLLHR *. * * * * * * * * * * * * * * * * * *             |
| GA   | PEDGALLGKIEKVRVLRNDRREGLMRSRVRGADAAQAKVLTFLDSHCECNEHWLEPLLER  |
| HP   | VKEDYTRVVCPVIDIINLDTFTYIESASELRGGFDWSLHFQWEQLSPEQ-KARRLDPTEP  |
|      | * ** **** * ** ** * * * * * * * * * * *   |
| GA   | VAEDRTRVVSPIIDVINMDNFQYVGASADLKGGFDWNLVFKWDYMTPEQRRSRQGNPVAP  |
| н    | PIRTPIIAGGLFVIDKAWFDYLGKYDMDMDIWGGENFEISFRVWMCGGSLEIVPCSRVGHV   |
|      | *, **, ******, ** . *, ****** **, ****** ****** ******, ******  |
| G    | A IKTPMIAGGLFVMDKFYFEELGKYDMMMDVWGGENLEISFRVWQCGGSLEIIPCSRVGHV  |

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|    | HP FRKKHPYVFPDGNANTYIKNTKRTAEVWMDEYKQYYYAARPFALERPFGNVESRLDLRKN |
|----|---|
|    | ***, ***, **, * , **, *, ********* . **** * * . *, **, *        |
|    | GA FRKQHPYTFPGGSGTVFARNTRRAAEVWMDEYKNFYYAAVPSARNVPYGNIQSRLELRKK |
|    |   |
|    | HP LRCQSFKWYLENIYPELSIPKESSIQKGNIRQRQKCLESQRQNNQETPNLKLSPCAKVKG |
| 5  | *. * ****** * . ***   |
|    | GA LSCKPFKWYLENVYPELRVPDHQDIAFGALQQGTNCLDTLGHFADGVVGVYECH       |
|    | HP EDAKSQVWAFTYTQQILQEELCLSVITLFPGAPVVLVLCKNGDDRQQWTKTGSHIEHI   |
|    | * **. * ***. * * * *. *   |
| 10 | GA NAGGNQEWALTKEKSVKHMDLCLTVVDRAPGSLIKLQGCRENDSRQKWEQIEGNSKLRHV |
|    |   |

 $HP\ ASHLCLDTDMFGDGTENGKEIVVNPCESSLMSQHWDMVSS$ 

GA GSNLCLDS---R-TAKSGGLSVEVCGPAL-SQQWKFTLNLQQ

of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA160076) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

## INDUSTRIAL APPLICABILITY

The present invention provides human proteins

25 having hydrophobic domains, DNAs encoding these proteins,

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expression vectors for these DNAs and eukaryotic cells expressing these DNAs. Since all of the proteins of the present invention are secreted or exist in the cell membrane, they are considered to be proteins controlling the proliferation and/or the differentiation of the cells. Accordingly, the proteins of the present invention can be employed as pharmaceuticals such as carcinostatic agents which act to control the proliferation and/or differentiation of the cells, or as antigens for preparing antibodies against these proteins. The DNAs of the present invention can be utilized as probes for the genetic diagnosis and gene sources for the gene therapy. Furthermore, the DNAs can be utilized for expressing these proteins in large quantities. Cells into which these genes are introduced to express these proteins can be utilized for detection of the corresponding receptors or ligands, screening of novel small molecule pharmaceuticals and the like. The antibody of the present invention can be utilized for the detection, quantification, purification and the like of the protein of the present invention.

The present invention also provides genes corresponding to the polynucleotide sequences disclosed herein. "Corresponding genes" are the regions of the genome that are transcribed to produce the mRNAs from which cDNA polynucleotide sequences are derived and may include

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contiguous regions of the genome necessary for the regulated expression of such genes. Corresponding genes may therefore include but are not limited to coding sequences, 5' and 3' untranslated regions, alternatively spliced exons, introns, promoters, enhancers, and silencer or suppressor elements. The corresponding genes can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include the preparation of probes or sequence information from the disclosed identification and/or amplification of genes in appropriate genomic libraries or other sources of genomic materials. An "isolated gene" is a gene that has been separated from the adjacent coding sequences, if any, present in the genome of the organism from which the gene was isolated.

Organisms that have enhanced, reduced, or modified of expression the gene(s) corresponding to the polynucleotide sequences disclosed herein are provided. The desired change in gene expression can be achieved through the use of antisense polynucleotides or ribozymes that bind and/or cleave the mRNA transcribed from the gene (Albert and Morris, 1994, Trends Pharmacol. Sci. 15(7): 250-254; Lavarosky et al., 1997, Biochem. Mol. Med. 62(1): 11-22; and Hampel, 1998, Prog. Nucleic Acid Res. Mol. Biol. 58: 1-39; all of which are incorporated by reference herein). Transgenic animals that have multiple copies of the gene(s)

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corresponding to the polynucleotide sequences disclosed herein, preferably produced by transformation of cells with genetic constructs that are stably maintained within the their transformed cells and progeny, are provided. Transgenic animals that have modified genetic control regions that increase or reduce gene expression levels, or that change temporal or spatial patterns of gene expression, are also provided (see European Patent No. 0 649 464 B1, incorporated by reference herein). In addition, organisms are provided in which the gene(s) corresponding to the polynucleotide sequences disclosed herein have partially or completely inactivated, through insertion of extraneous sequences into the corresponding gene(s) or through deletion of all or part of the corresponding gene(s). Partial or complete gene inactivation can be accomplished through insertion, preferably followed by imprecise excision, of transposable elements (Plasterk, 1992, Bioessays 14(9): 629-633; Zwaal et al., 1993, Proc. Natl. Acad. Sci. USA 90(16): 7431-7435; Clark et al., 1994, Proc. Natl. Acad. Sci. USA 91(2): 719-722; all of which are incorporated by reference herein), or through homologous recombination, preferably detected by positive/negative genetic selection strategies (Mansour et al., 1988, Nature 336: 348-352; U.S. Patent Nos. 5,464,764; 5,487,992; 5,627,059; 5,631,153; 5,614, 396; 5,616,491; and 5,679,523; all of which are

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incorporated by reference herein). These organisms with altered gene expression are preferably eukaryotes and more preferably are mammals. Such organisms are useful for the development of non-human models for the study of disorders involving the corresponding gene(s), and for the development of assay systems for the identification of molecules that interact with the protein product(s) of the corresponding gene(s).

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Where the protein of the present invention is membrane-bound (e.g., is a receptor), the present invention also provides for soluble forms of such protein. In such forms part or all of the intracellular and transmembrane domains of the protein are deleted such that the protein is fully secreted from the cell in which it is expressed. The intracellular and transmembrane domains of proteins of the invention can be identified in accordance with known techniques for determination of such domains from sequence information.

invention include proteins with amino acid sequence lengths that are at least 25% (more preferably at least 50%, and most preferably at least 75%) of the length of a disclosed protein and have at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% or 95% identity) with that disclosed protein, where

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sequence identity is determined by comparing the amino acid sequences of the proteins when aligned so as to maximize overlap and identity while minimizing sequence gaps. Also included in the present invention are proteins and protein fragments that contain a segment preferably comprising 8 or more (more preferably 20 or more, most preferably 30 or more) contiguous amino acids that shares at least 75% sequence identity (more preferably, at least 85% identity; most preferably at least 95% identity) with any such segment of any of the disclosed proteins.

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Species homologs of the disclosed polynucleotides and proteins are also provided by the present invention. As used herein, a "species homologue" is a protein or polynucleotide with a different species of origin from that of a given protein or polynucleotide, but with significant sequence similarity to the given protein or polynucleotide, as determined by those of skill in the art. Species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source from the desired species.

The invention also encompasses allelic variants of the disclosed polynucleotides or proteins; that is, naturally-occurring alternative forms of the isolated polynucleotide which also encode proteins which are identical, homologous, or related to that encoded by the

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polynucleotides.

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The invention also includes polynucleotides with sequences complementary to those of the polynucleotides disclosed herein.

The present invention also includes polynucleotides capable of hybridizing under reduced stringency conditions, more preferably stringent conditions, and most preferably highly stringent conditions, to polynucleotides described herein. Examples of stringency conditions are shown in the table below: highly stringent & 10 conditions are those that are at least as stringent as, for example, conditions A-F; stringent conditions are at least as stringent as, for example, conditions G-L; and reduced stringency conditions are at least as stringent as, for example, conditions M-R. 15

Table 29

| Stringency | Poly-      | Hybrid | Hybridization Temperature | Wash                    |
|------------|------------|--------|---------------------------|-------------------------|
| Condition  | nucleotide | Length | and Buffer <sup>†</sup>   | Temperature             |
|            | Hybrid '   | (bp) * | ·                         | and Buffer              |
| A          | DNA: DNA   | ≥50    | 65°C; 1×SSC -or-          | 65°C; ·                 |
|            |            |        | 42°C; 1×SSC,50%           | 0.3×SSC                 |
|            |            |        | formamide                 |                         |
| В          | DNA: DNA   | <50    | T <sub>B</sub> *; 1×SSC   | T <sub>B</sub> *; 1×SSC |
| С          | DNA: RNA   | ≥50    | 67°C; 1×SSC -or-          | 67°C;                   |
|            |            |        | 45°C; 1×SSC,50%           | 0.3×SSC                 |
|            |            |        | formamide                 |                         |
| D          | DNA: RNA   | <50    | T <sub>D</sub> *; 1×SSC   | Tp*; 1×SSC              |
| E          | RNA: RNA   | ≥50    | 70°C; 1×SSC -or-          | 70°C;                   |
| 1          |            |        | 50°C; 1×SSC,50%           | 0.3×SSC                 |
|            |            |        | formamide                 |                         |
| F          | RNA: RNA   | <50    | T <sub>F</sub> *; 1×SSC   | Tr*; 1×SSC              |
| G          | DNA: DNA   | ≥50    | 65°C; 4×SSC -or-          | 65°C; 1×SSC             |
|            |            |        | 42°C; 4×SSC,50%           |                         |
| 4          |            |        | formamide                 |                         |
| Н          | DNA: DNA   | <50    | T <sub>H</sub> *; 4×SSC   | T <sub>H</sub> *; 4×SSC |
| I          | DNA: RNA   | ≥50    | 67°C; 4×SSC -or-          | 67°C; 1×SSC             |
|            |            |        | 45°C; 4×SSC,50%           |                         |
|            |            |        | formamide                 | •                       |
| J          | DNA: RNA   | <50    | T <sub>J</sub> *; 4×SSC   | T <sub>J</sub> *; 4×SSC |
| K          | RNA: RNA   | ≥50    | 70°C; 4×SSC -or-          | 67°C; 1×SSC             |
|            |            |        | 50°C; 4×SSC,50%           |                         |
|            |            |        | formamide                 |                         |
| L          | RNA: RNA   | <50    | T <sub>L</sub> *; 2×SSC   | T <sub>L</sub> *; 2×SSC |
| М          | DNA : DNA  | ≥50    | 50°C; 4×SSC -or-          | 50°C; 2×SSC             |
|            |            |        | 40°C; 6×SSC,50%           |                         |
|            |            |        | formamide                 |                         |
| N          | DNA: DNA   | <50    | T <sub>N</sub> *; 6×SSC   | T <sub>N</sub> *; 6×SSC |
| 0          | DNA: RNA   | ≥50    | 55°C; 4×SSC -or-          | 55°C; 2×SSC             |
|            |            |        | 42°C; 6×SSC,50%           |                         |
|            |            |        | formamide                 |                         |
| P          | DNA: RNA   | <50    | Tp*; 6×SSC                | Tp*; 6×SSC              |
| Q          | RNA: RNA   | ≥50    | 60°C; 4×SSC -or-          | 60°C; 2×SSC             |
|            |            |        | 45°C; 6×SSC,50%           |                         |
|            |            |        | formamide                 |                         |
| R          | RNA: RNA   | <50    | T <sub>R</sub> *; 4×SSC   | T <sub>R</sub> *; 4×SSC |

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- ‡: The hybrid length is that anticipated for the hybridized region(s) of the hybridizing polynucleotides.

  When hybridizing a polynucleotide to a target polynucleotide of unknown sequence, the hybrid length is assumed to be that of the hybridizing polynucleotide. When polynucleotides of known sequence are hybridized, the hybrid length can be determined by aligning the sequences of the polynucleotides and identifying the region or regions of optimal sequence complementarity.
- t: SSPE (1×SSPE is 0.15M NaCl, 10mM NaH<sub>2</sub>PO<sub>4</sub>, and 1.25mM EDTA, pH7.4) can be substituted for SSC (1×SSC is 0.15M NaCl and 15mM sodium citrate) in the hybridization and wash buffers; washes are performed for 15 minutes after hybridization is complete.
- \*T<sub>B</sub> T<sub>R</sub>: The hybridization temperature for hybrids
  anticipated to be less than 50 base pairs in length should
  be 5-10°C less than the melting temperature (T<sub>m</sub>) of the
  hybrid, where T<sub>m</sub> is determined according to the following
  equations. For hybrids less than 18 base pairs in length,

  T<sub>m</sub>(°C)=2(#of A + T bases) + 4(# of G + C bases). For hybrids
  between 18 and 49 base pairs in length, T<sub>m</sub>(°C)=81.5 +
  16.6(log<sub>10</sub>[Na<sup>+</sup>]) + 0.41 (%G+C) (600/N), where N is the
  number of bases in the hybrid, and [Na<sup>+</sup>] is the concentration
  of sodium ions in the hybridization buffer ([Na<sup>+</sup>] for
  1×SSC=0.165M).

Additional examples of stringency conditions for polynucleotide hybridization are provided in Sambrook, J., E.F. Fritsch, and T. Maniatis, 1989, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, chapters 9 and 11, and Current Protocols in Molecular Biology, 1995, F.M. Ausubel et al., eds., John Wiley & Sons, Inc., sections 2.10 and 6.3-6.4, incorporated herein by reference.

Preferably, each such hybridizing polynucleotide has a length that is at least 25% (more preferably at least 50%, and most preferably at least 75%) of the length of the polynucleotide of the present invention to which it hybridizes, and has at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% or 95% identity) with the polynucleotide of the present invention to which it hybridizes, where sequence identity is determined by comparing the sequences of the hybridizing polynucleotides when aligned so as to maximize overlap and identity while minimizing sequence gaps.

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## CLAIMS

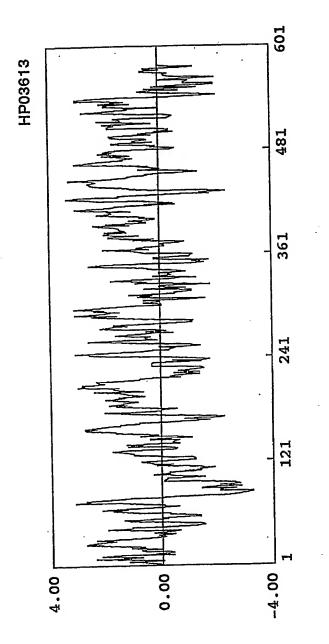
1. A protein comprising any one of amino acid sequences selected from the group consisting of SEQ ID NOS: 1 to 10, 31 to 40, 61 to 70, 91 to 100 and 121 to 130.

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- 2. An isolated DNA encoding the protein according to Claim 1.
- 3. An isolated cDNA comprising any one of base sequences selected from the group consisting of SEQ ID NOS: 11 to 20, 41 to 50, 71 to 80, 101 to 110 and 131 to 140.
  - 4. The cDNA according to Claim 3 consisting of any one of base sequences selected from the group consisting of SEQ ID NOS: 21 to 30, 51 to 60, 81 to 90, 111 to 120 and 141 to 150.
- 5. An expression vector that is capable of expressing the DNA according to any one of Claim 2 to Claim 4 by in vitro translation or in eukaryotic cells.
  - 6. A transformed eukaryotic cell that is capable of expressing the DNA according to any one of Claim 2 to Claim 4 and of producing the protein according to Claim 1.
  - 7. An antibody directed to the protein according to Claim 1.

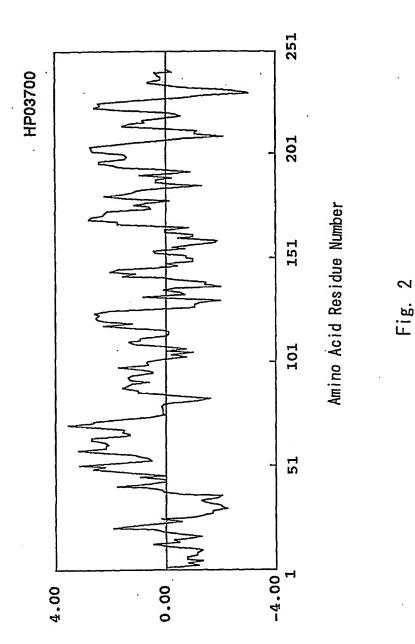


Amino Acid Residue Number

Hydrophilicity/Hydrophobicity

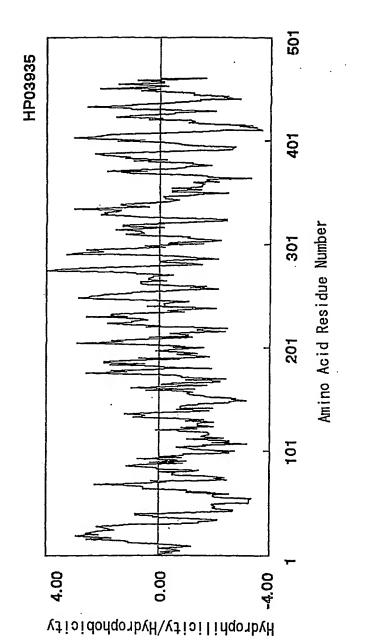
(P)

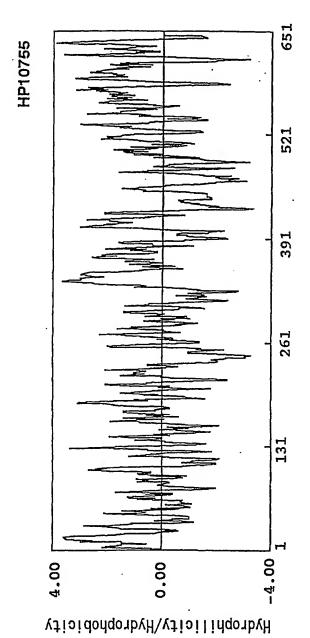
2/50



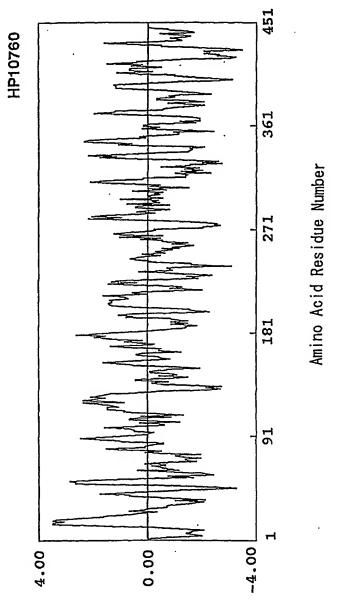
Hydrophilicity/Hydrophobicity

3/50

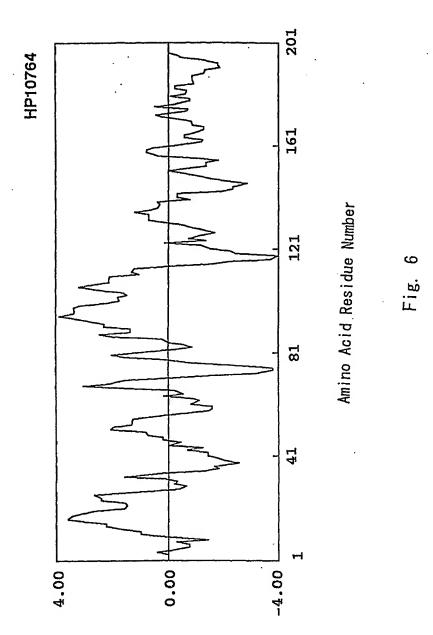




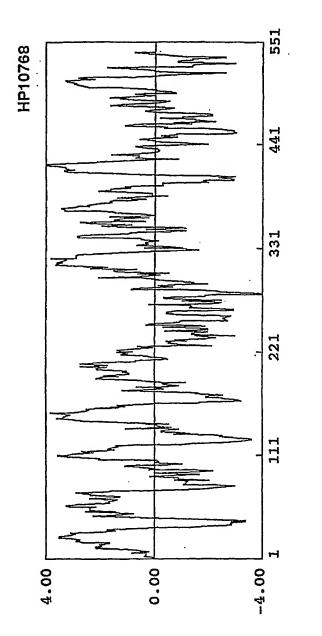
Amino Acid Residue Number



Hydrophilicity/Hydrophobicity



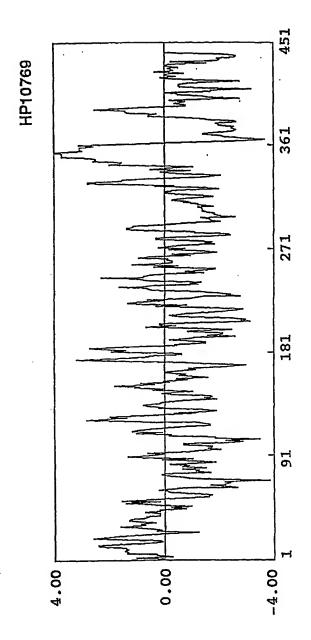
Hydrophilicity/Hydrophobicity



Amino Acid Residue Number

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Hydrophilicity/Hydrophobicity



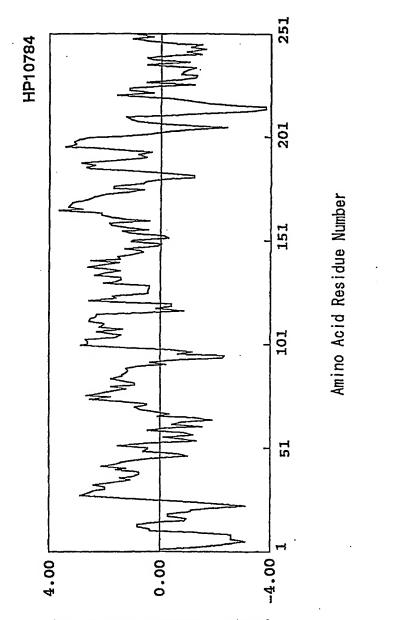
Hydrophilicity/Hydrophobicity

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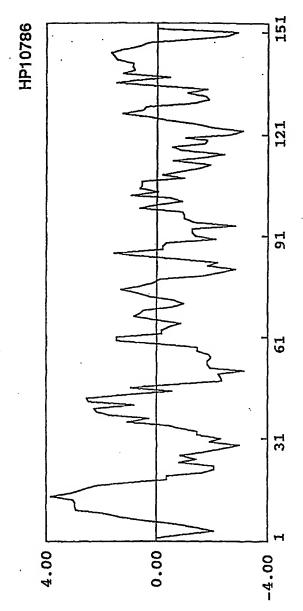
Amino Acid Residue Number

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Hydrophilicity/Hydrophobicity



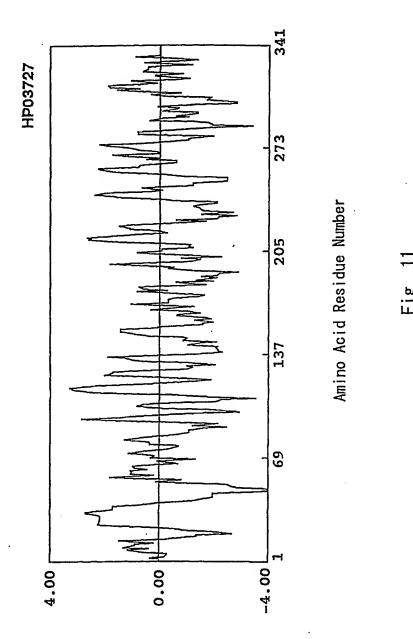
Hydrophilicity/Hydrophobicity

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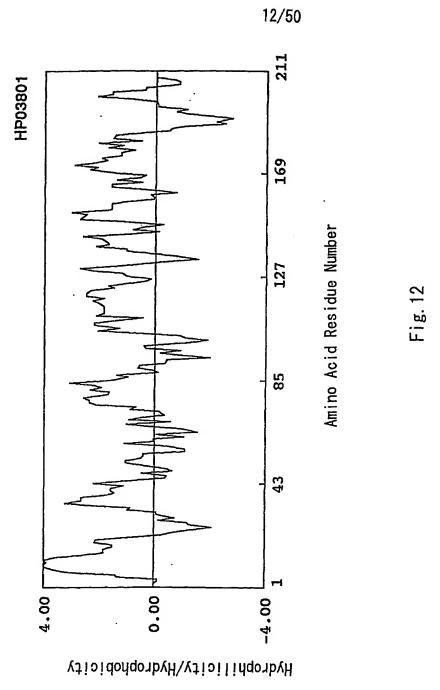
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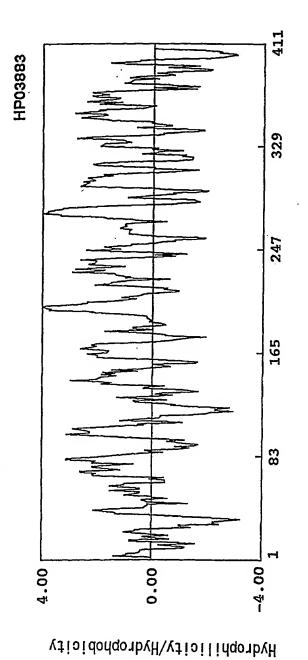
Fig.

Amino Acid Residue Number



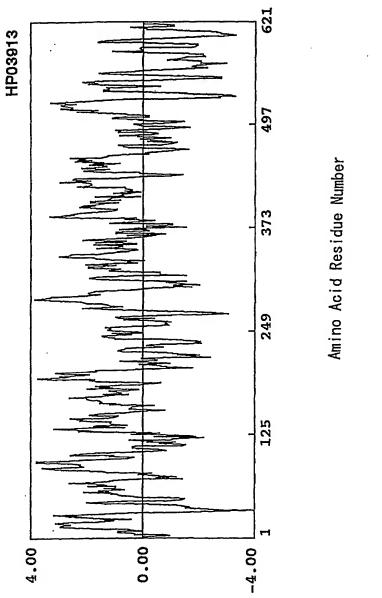
Hydrophilicity/Hydrophobicity





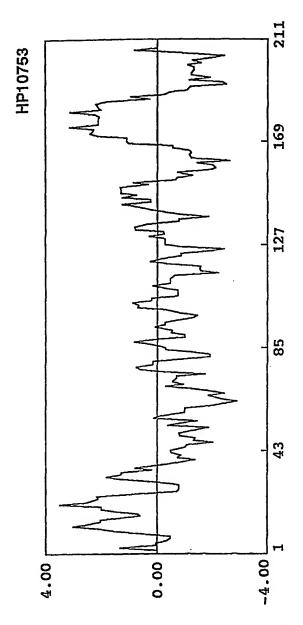
Amino Acid Residue Number

0

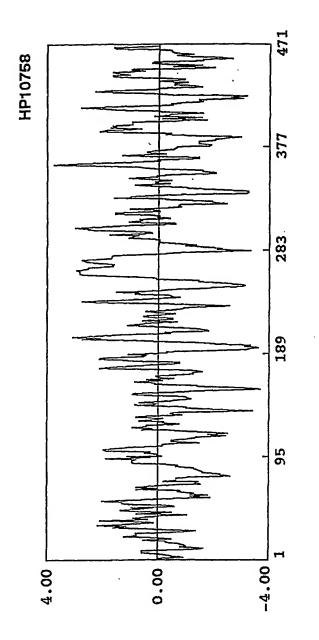


Hydrophilicity/Hydrophobicity

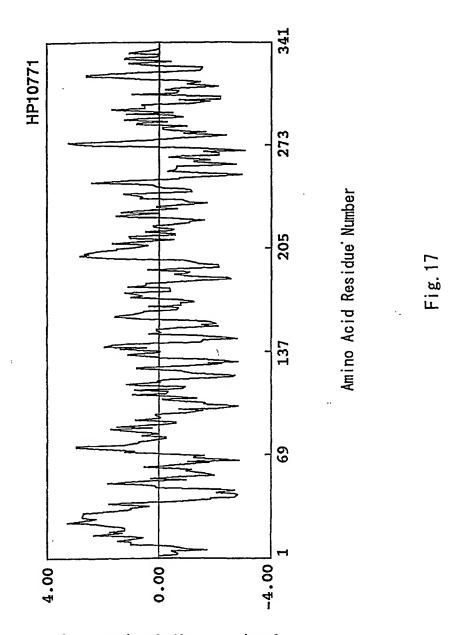
Fig. 14



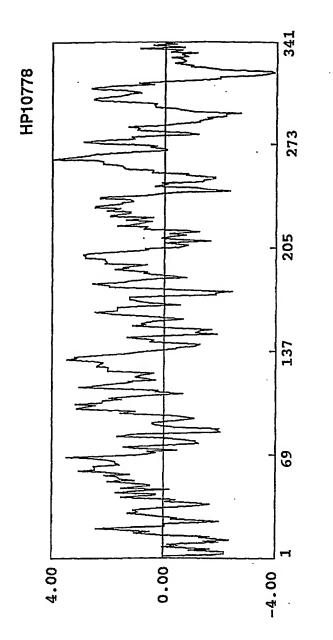
Hydrophilicity/Hydrophobicity



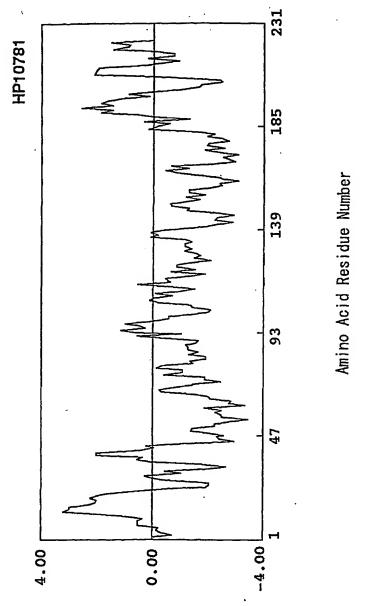
Hydrophilicity/Hydrophobicity



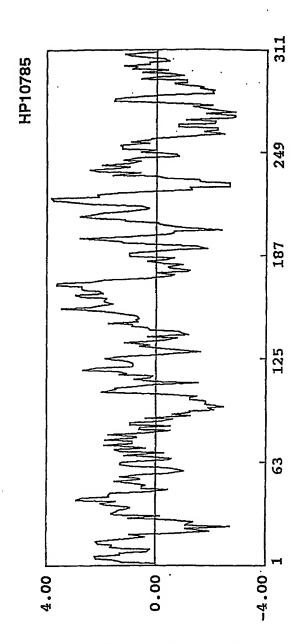
 $H \lambda d rophilicit y/H y d rophobicit y$ 



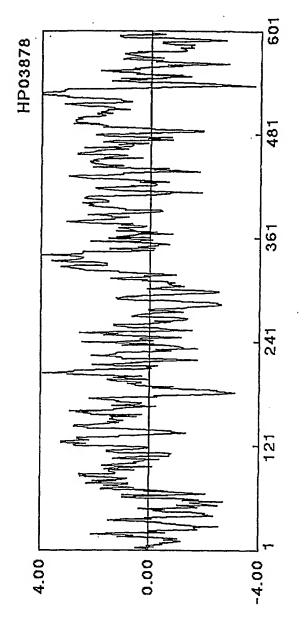
ΗλακορμίΙισιτη/Ηγακορμορίσιτη



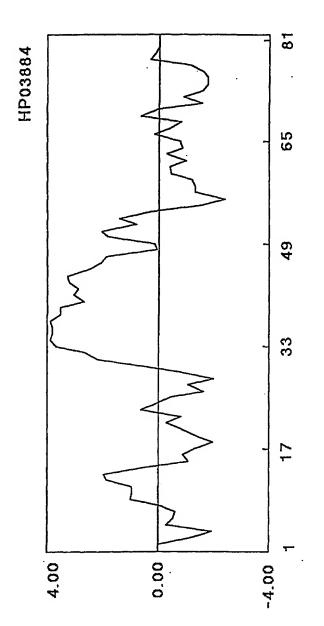
Hydrophilicity/Hydrophobicity



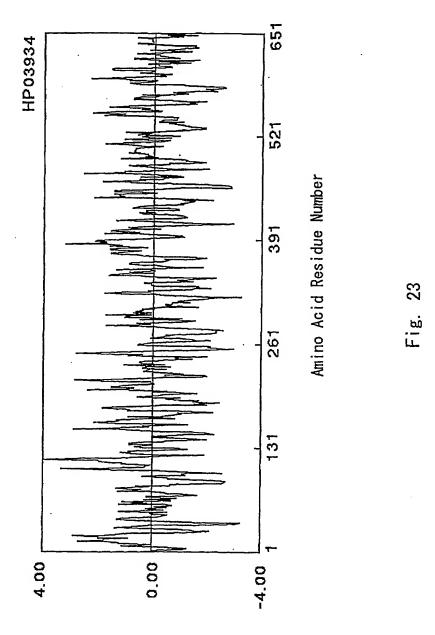
 ${\it H} \lambda {\it q} Lobhilicity/{\it H} \lambda {\it d} Lobhobicity$ 



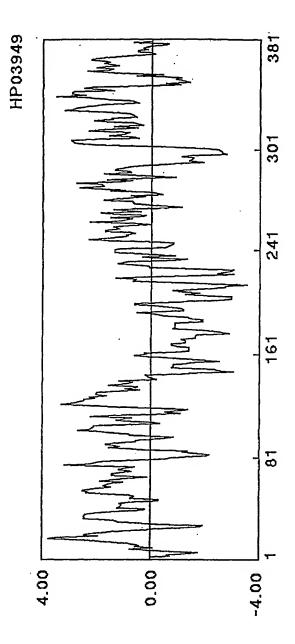
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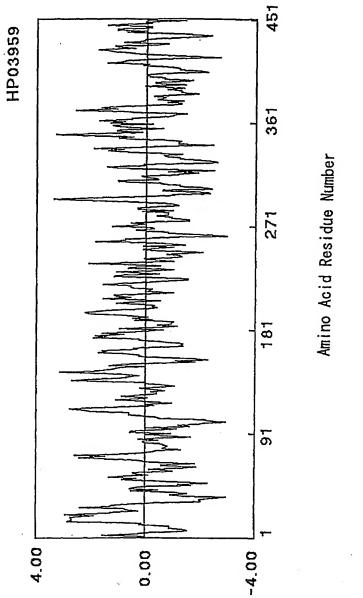
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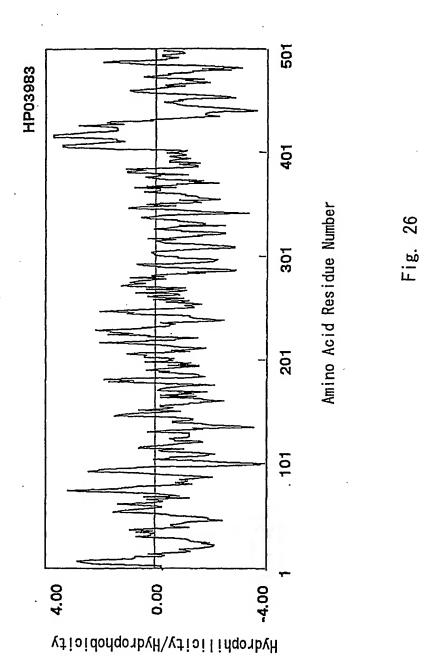
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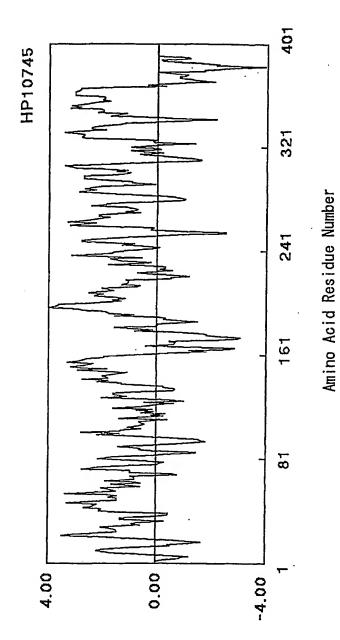
Amino Acid Residue Number



25







Hydrophilicity/Hydrophobicity



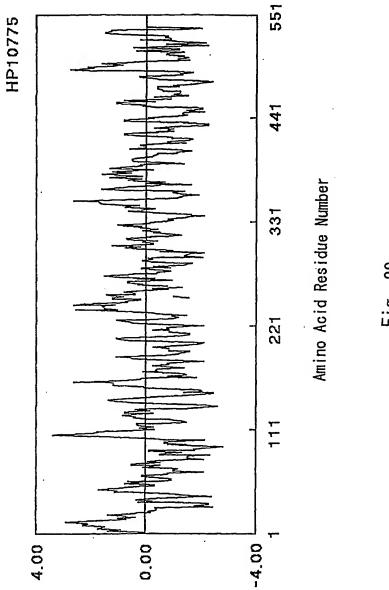
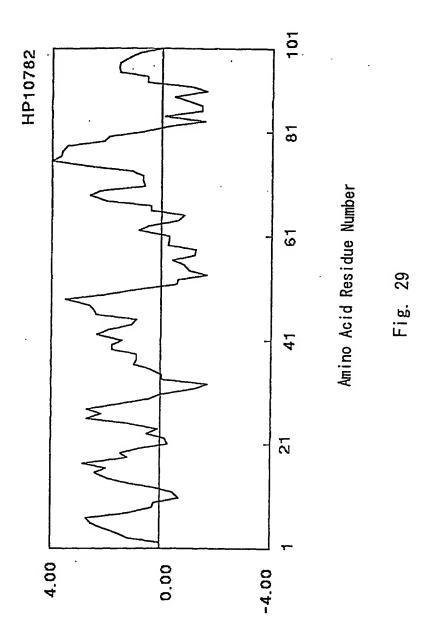
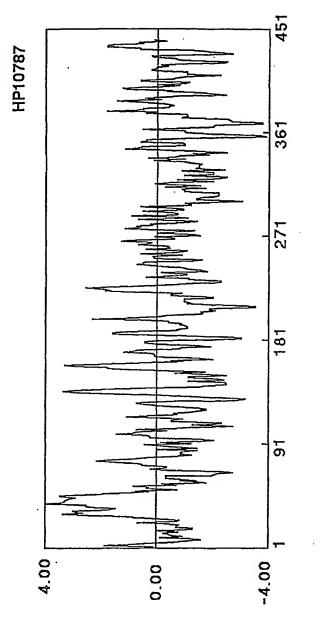


Fig. 28

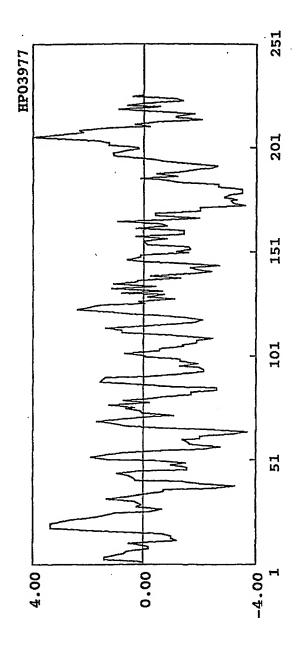


Hydrophilicity/Hydrophobicity



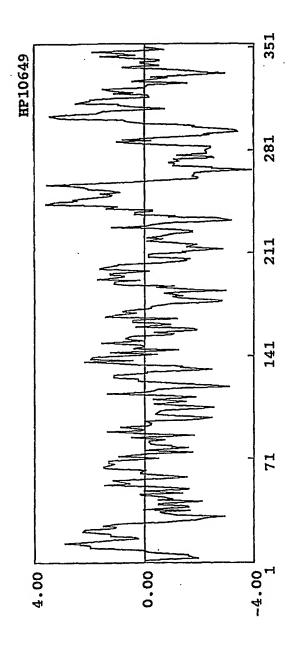
 ${\tt H} \lambda {\tt qtob} {\tt licit} \lambda \backslash {\tt H} \lambda {\tt qtob} {\tt loif} \lambda$ 

Fig. 30

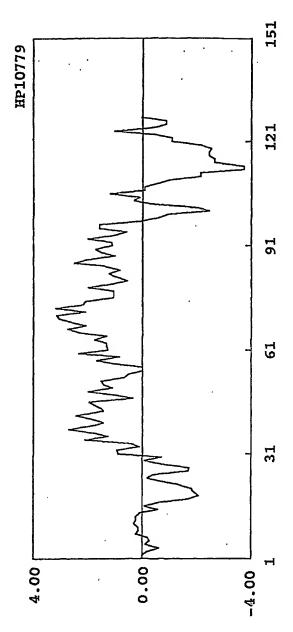


Amino Acid Residue Number

 $H\lambda drophilicity/Hy drophobicity$ 

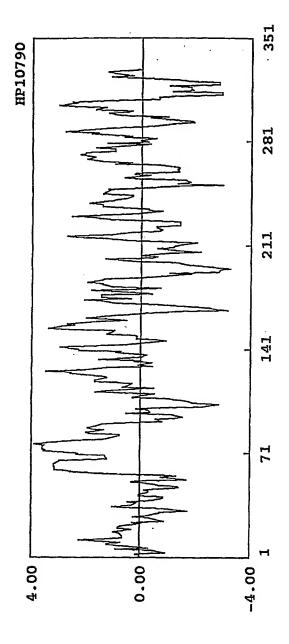


Amino Acid Residue Number

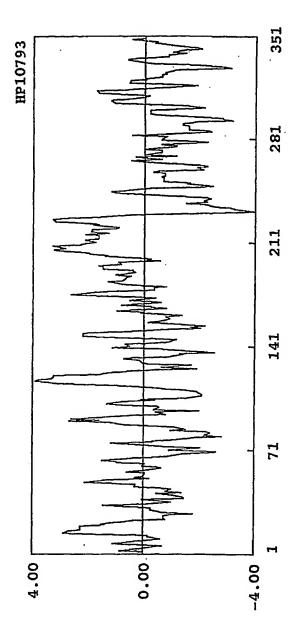


Hydrophilicity/Hydrophobicity

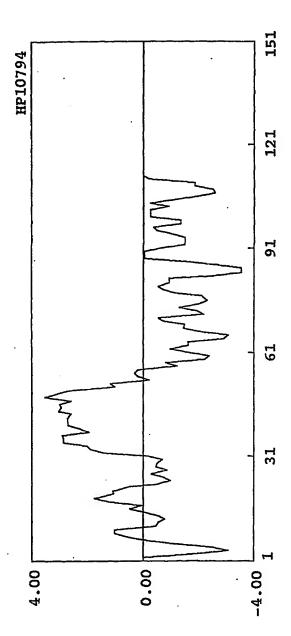
·ig. 33



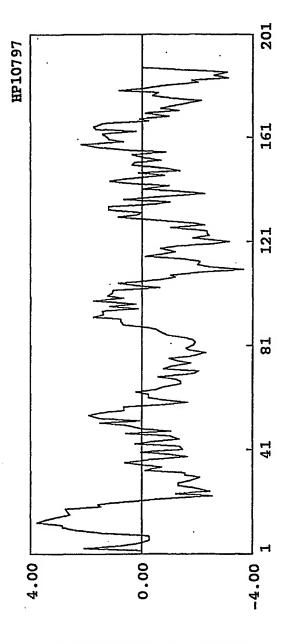
Amino Acid Residue Number



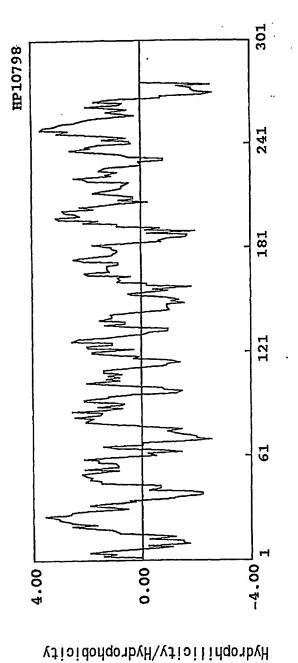
Hydrophilicity/Hydrophobicity



Hydrophilicity/Hydrophobicity

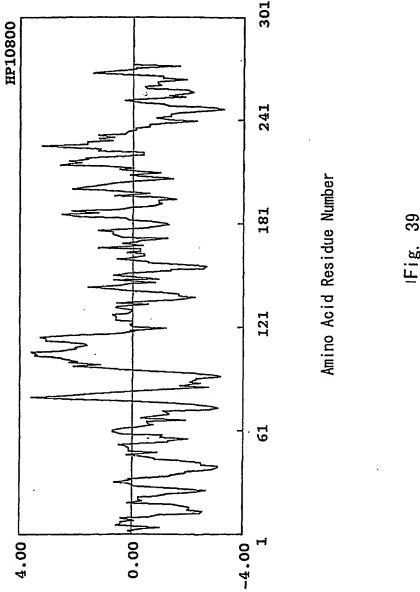


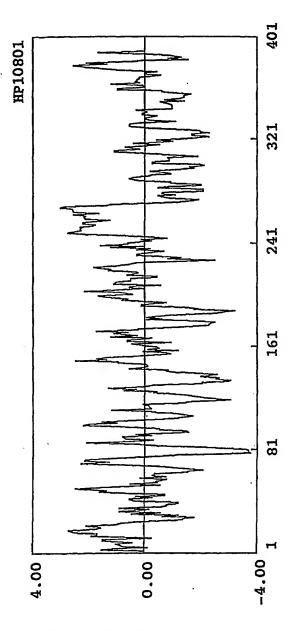
Amino Acid Residue Number



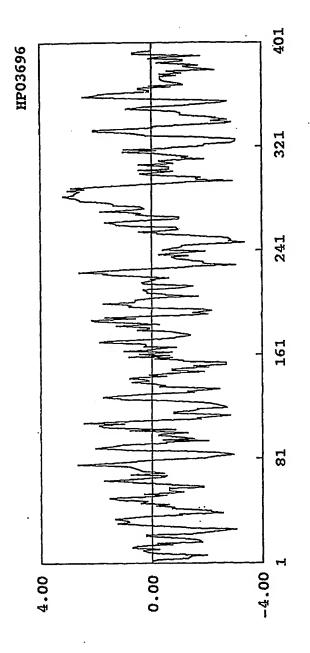
Amino Acid Residue Number

39/50

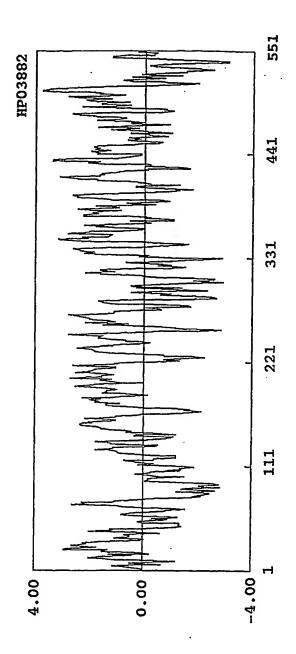




Hydrophilicity/Hydrophobicity



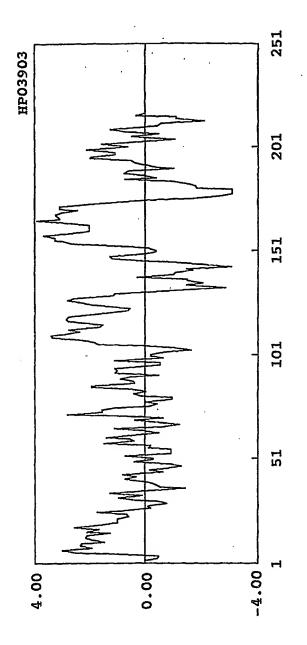
Amino Acid Residue Number



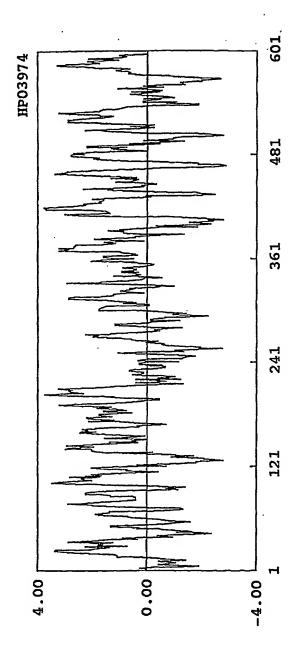
 $H\lambda drophilicity/Hydrophobicity\\$ 

Fig 42

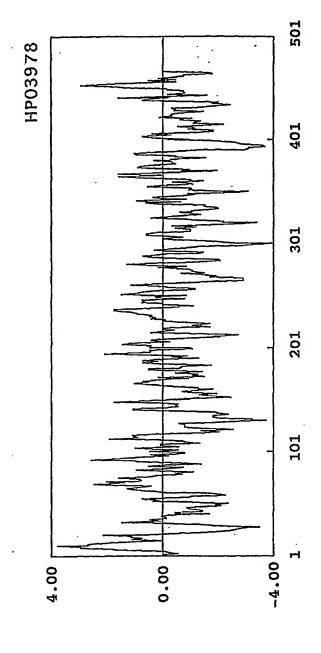
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Amino Acid Residue Number

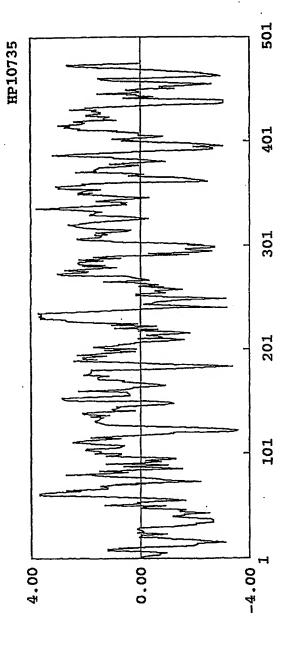


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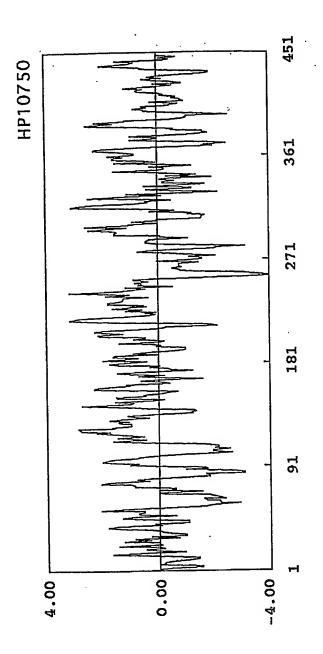
Amino Acid Residue Number

ig. 45

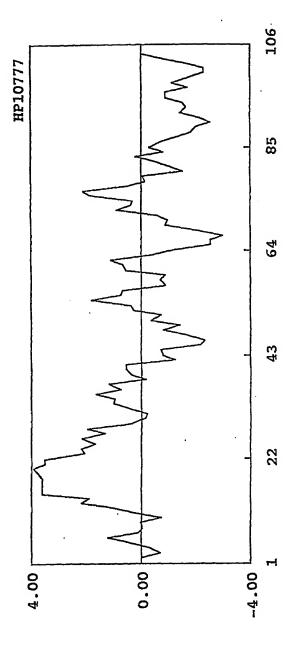


Amino Acid Residue Number Fig. 46

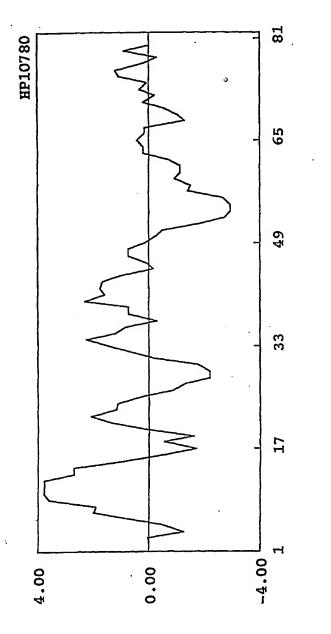
 ${\tt H} \lambda {\tt q} \kappa {\tt obpilicity} {\tt H} \lambda {\tt q} \kappa {\tt obpopicity}$ 



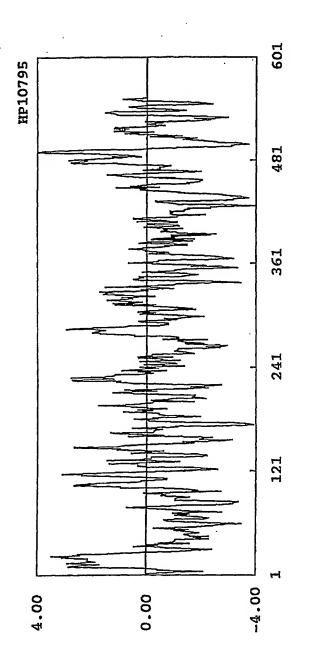
Amino Acid Residue Number



Amino Acid Residue Number Fig. 48



Amino Acid Residue Number



Amino Acid Residue Number

# 1 /346

### SEQUENCE LISTING

<110> Protegene Inc.,

Sagami Chemical Research Center

5

<120> Human proteins having hydrophobic domains and DNAs encoding these proteins

<130> 662248

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<150> JP 2000-585

<151> 2000-01-06

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2 /346

<160> 150

<210> 1

<211> 578

5 <212> PRT

<213> Homo sapiens

<400> i

1

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5

15

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20 25 3

10

Thr Gln Ser Met Leu Glu Asn Phe Ser Ala Ala Val Pro Ser His Arg

35 40 45

Cys Trp Ala Pro Leu Leu Asp Asn Ser Thr Ala Gln Ala Ser Ile Leu

15 50 55 60

Gly Ser Leu Ser Pro Glu Ala Leu Leu Ala Ile Ser Ile Pro Pro Gly

65 70 75 80

Pro Asn Gln Arg Pro His Gln Cys Arg Arg Phe Arg Gln Pro Gln Trp

85 90 95

20 Gln Leu Leu Asp Pro Asn Ala Thr Ala Thr Ser Trp Ser Glu Ala Asp

100 105 110

Thr Glu Pro Cys Val Asp Gly Trp Val Tyr Asp Arg Ser Ile Phe Thr

115 120 125

Ser Thr Ile Val Ala Lys Trp Asn Leu Val Cys Asp Ser His Ala Leu

25 130 135 140

|    | Lys | Pro | Met | Ala | Gln | Ser | Ile | Tyr | Leu | Ala | Gly | Ile | Leu | Val | Gly | Ala |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
|    | Ala | Ala | Cys | Gly | Pro | Ala | Ser | Asp | Arg | Phe | Gly | Arg | Arg | Leu | Val | Leu |
|    |     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
| 5  | Thr | Trp | Ser | Tyr | Leu | Gln | Met | Ala | Val | Met | Gly | Thr | Ala | Ala | Ala | Phe |
|    |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
|    | Ala | Pro | Ala | Phe | Pro | Val | Tyr | Cys | Leu | Phe | Arg | Phe | Leu | Leu | Ala | Phe |
|    |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
|    | Ala | Val | Ala | Gly | Val | Met | Met | Asn | Thr | Gļy | Thr | Leu | Arg | Arg | Ser | Leu |
| LO |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
|    | Thr | Trp | Arg | His | Ala | Gly | Gly | Leu | His | Ala | Gly | Ser | Arg | Ala | Glu | Pro |
|    | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
|    | Leu | Gly | Leu | Leu | Ala | Val | Met | Glu | Trp | Thr | Ala | Ala | Arg | Ala | Arg | Pro |
|    |     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |
| .5 | Leu | Val | Met | Thr | Leu | Asn | Ser | Leu | Gly | Phe | Ser | Phe | Gly | His | Gly | Leu |
|    |     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |
|    | Thr | Ala | Ala | Val | Ala | Tyr | Gly | Val | Arg | Asp | Trp | Thr | Leu | Leu | Gln | Leu |
|    |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |
|    | Val | Val | Ser | ۷al | Pro | Phe | Phe | Leu | Cys | Phe | Leu | Tyr | Ser | Trp | Trp | Leu |
| 20 |     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |
|    | Ala | Glu | Ser | Ala | Arg | Trp | Leu | Leu | Thr | Thr | Gly | Arg | Leu | Asp | Trp | Gly |
|    | 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |
|    | Leu | Gln | Glu | Leu | Trp | Arg | Val | Ala | Ala | Ile | Asn | Gly | Lys | Gly | Ala | Val |
|    |     |     |     |     | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |
| 25 | Gln | Asp | Thr | Leu | Thr | Pro | Glu | Val | Leu | Leu | Ser | Ala | Met | Ara | Glu | Glu |

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Gi

|    |     |     |     | 340 |     |     |       |     | 345 |      |     |     |     | 350   |             |      |
|----|-----|-----|-----|-----|-----|-----|-------|-----|-----|------|-----|-----|-----|-------|-------------|------|
|    | Leu | Ser | Met | Gly | Gln | Pro | Pro   | Ala | Ser | Leu  | Gly | Thr | Leu | Leu   | Arg         | Met  |
|    |     |     | 355 |     |     |     |       | 360 |     |      |     |     | 365 |       |             |      |
|    | Pro | Gly | Leu | Arg | Phe | Arg | Thr   | Cys | Ile | Ser  | Thr | Leu | Cys | Trp   | Phe         | Ala  |
| 5  |     | 370 |     |     |     |     | 375   |     |     |      |     | 380 |     |       |             |      |
|    | Phe | Gly | Phe | Thr | Phe | Phe | Gly   | Leu | Ala | Leu  | Asp | Leu | Gln | Ala   | Leu         | Gly  |
|    | 385 |     |     |     |     | 390 |       |     |     |      | 395 |     |     |       |             | 400  |
|    | Ser | Asn | Ile | Phe | Leu | Leu | Gln   | Met | Phe | Ile  | Gly | Val | Val | Asp   | Ile         | Pro  |
|    |     |     |     |     | 405 |     |       |     |     | 410  |     |     |     |       | 415         |      |
| 10 | Ala | Lys | Met | Gly | Ala | Leu | Leu   | Leu | Leu | Ser  | His | Leu | Gly | Arg   | Arg         | Pro  |
|    |     |     |     | 420 |     |     |       |     | 425 |      |     |     |     | 430   |             |      |
|    | Thr | Leu | Ala | Ala | Ser | Leu | Leu   | Leu | Ala | Gly  | Leu | Cys | Ile | Leu   | Ala         | Asn  |
|    |     |     | 435 |     |     |     |       | 440 |     |      |     |     | 445 |       |             |      |
|    | Thr | Leu | Val | Pro | His | Glu | Met   | Gly | Ala | Leu  | Arg | Ser | Ala | Leu   | Ala         | Val  |
| 15 |     | 450 |     |     |     |     | 455   |     |     |      |     | 460 |     |       |             |      |
|    | Leu | Gly | Leu | Gly | Gly | Val | Gly   | Ala | Ala | Phe  | Thr | Cys | Ile | Thr   | Ile         | Tyr  |
|    | 465 |     |     |     |     | 470 |       |     |     |      | 475 |     |     |       |             | 480  |
|    | Ser | Ser | Glu | Leu | Phe | Pro | Thr   | Val | Leu | Arg  | Met | Thr | Ala | Val   | Gly         | Leu  |
|    |     |     |     |     | 485 |     |       |     |     | 490  |     |     |     |       | 495         |      |
| 20 | Gly | Gln | Met | Ala | Ala | Arg | Gly   | Gly | Ala | Ile  | Leu | Gly | Pro | Leu   | Val         | Arq  |
|    |     |     |     | 500 |     | •   | _     | _   | 505 |      |     | -   |     | 510   |             |      |
|    | Leu | Leu | Glv | Val | His | Glv | Pro   | Tro | Leu | Pro  | Leu | Leu | Val |       |             | Thr  |
|    |     |     | 515 |     |     |     |       | 520 |     |      |     |     | 525 | -1-   | <b>-</b> _1 |      |
|    | Val | Pro |     | Leu | Ser | Glv | T'611 |     | Ala | ],en | Len | Ten |     | Gl 11 | ሞኮ~         | מנט  |
| 25 |     | 530 |     | 204 |     | 1   | 535   |     |     |      | 204 | 540 | 110 | GIU   | ***         | 0111 |
|    |     |     |     |     |     |     |       |     |     |      |     |     |     |       |             |      |

|    | ser  | ren   | Pro   | Leu   | Pro | Asp | Thr | тте | GIN | Asp | Val | GIn | Asn | GIn | Ala | Val |
|----|------|-------|-------|-------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | 545  |       |       |       |     | 550 |     |     |     |     | 555 |     |     |     |     | 560 |
|    | Lys  | Lys   | Ala   | Thr   | His | Gly | Thr | Leu | Gly | Asn | Ser | Val | Leu | Lys | Ser | Thr |
|    |      |       |       |       | 565 |     |     |     |     | 570 |     |     |     |     | 575 |     |
| 5  | Gln  | Phe   |       |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    |      |       |       |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <210 | 0> 2  |       |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <21  | 1> 24 | 43    |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <212 | 2> PI | RT    |       |     |     |     |     |     |     |     |     |     |     |     |     |
| 10 | <213 | 3> Ho | omo s | sapie | ens |     |     |     |     |     |     |     |     |     |     |     |
|    | <400 | )> 2  |       |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | Met  | Ser   | Arg   | Ser   | Pro | Leu | Asn | Pro | Ser | Gln | Leu | Arg | Ser | Val | Gly | Ser |
|    | 1    |       |       |       | 5   |     |     |     |     | 10  |     |     | -   |     | 15  |     |
|    | Gln  | Asp   | Ala   | Leu   | Ala | Pro | Leu | Pro | Pro | Pro | Ala | Pro | Gln | Asn | Pro | Ser |
| 15 |      |       |       | 20    |     |     |     |     | 25  |     |     |     |     | 30  |     | -   |
|    | Thr  | His   | Ser   | Trp   | Asp | Pro | Leu | Суз | Gly | Ser | Leu | Pro | Trp | Gly | Leu | Ser |
|    |      |       | 35    |       |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
|    | Cys  | Leu   | Leu   | Ala   | Leu | Gln | His | Val | Leu | Val | Met | Ala | Ser | Leu | Leu | Cys |
|    |      | 50    |       |       |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
| 20 | Val  | Ser   | His   | Leu   | Leu | Leu | Leu | Cys | Ser | Leu | Ser | Pro | Gly | Gly | Leu | Ser |
|    | 65   |       |       |       |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
|    | Tyr  | Ser   | Pro   | Ser   | Gln | Leu | Leu | Ala | Ser | Ser | Phe | Phe | Ser | Cys | Gly | Met |
|    |      |       |       |       | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
|    | Ser  | Thr   | Ile   | Leu   | Gln | Thr | Trp | Met | Gly | Ser | Arg | Leu | Pro | Leu | Val | Gln |
| 25 |      |       |       | 100   |     |     |     |     | 105 |     |     |     |     | 110 |     |     |

|    | Ala  | Pro   | Ser  | Leu   | Glu | Phe | Leu | Ile | Pro | Ala | Leu | Val | Leu | Thr | Ser | Gln |
|----|------|-------|------|-------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    |      |       | 115  |       | •   |     |     | 120 |     |     |     |     | 125 |     |     |     |
|    | Lys  | Leu   | Pro  | Arg   | Ala | Ile | Gln | Thr | Pro | Gly | Asn | Ser | Ser | Leu | Met | Leu |
|    |      | 130   |      |       |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
| 5  | His  | Leu   | Cys  | Arg   | Gly | Pro | Ser | Cys | His | Gly | Leu | Gly | His | Trp | Asn | Thr |
|    | 145  |       |      |       |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
|    | Ser  | Leu   | Gln  | Glu   | Val | Ser | Gly | Ala | Val | Val | Val | Ser | Gly | Leu | Leu | Gln |
|    |      |       |      |       | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
|    | Gly  | Met   | Met  | Gly   | Leu | Leu | Gly | Ser | Pro | Gly | His | Val | Phe | Pro | His | Cys |
| 10 |      |       |      | 180   |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
|    | Gly  | Pro   | Leu  | Val   | Leu | Ala | Pro | Ser | Leu | Val | Val | Ala | Gly | Leu | Ser | Ala |
|    |      |       | 195  |       |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
|    | His  | Arg   | Glu  | Val   | Ala | Gln | Phe | Cys | Phe | Thr | His | Trp | Gly | Leu | Ala | Leu |
|    |      | 210   |      |       |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
| 15 | Leu  | Tyr   | Val  | Ser   | Pro | Glu | Arg | Arg | Gly | Met | Val | Pro | Ser | Gly | Gly | Val |
|    | 225  |       |      |       |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
|    | Trp  | Gly   | Asp  |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    |      |       |      |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <210 | )> 3  |      |       |     |     |     |     |     |     |     |     |     |     |     |     |
| 20 | <213 | 1> 46 | 51   |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <212 | 2> PF | T    |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <213 | 3> нс | mo s | sapie | ens |     |     |     |     |     |     |     |     |     |     |     |
|    | <400 | )> 3  |      |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | Met  | Ala   | Pro  | Gln   | Ser | Leu | Pro | Ser | Ser | Arg | Met | Ala | Pro | Leu | Gly | Met |
| 25 | 1    |       |      |       | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |

|    | Leu | Leu | Gly | Leu | Leu | Met | Ala | Ala | Cys | Phe | Thr | Phe | Cys | Leu | Ser | His |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    |     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
|    | Gln | Asn | Leu | Lys | Glu | Phe | Ala | Leu | Thr | Asn | Pro | Glu | Lys | Ser | Ser | Thi |
|    |     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
| 5  | Lys | Glu | Thr | Glu | Arg | Lys | Glu | Thr | Lys | Ala | Glu | Glu | Glu | Leu | Asp | Ala |
|    |     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
|    | Glu | Val | Leu | Glu | Val | Phe | His | Pro | Thr | His | Glu | Trp | Gln | Ala | Leu | Glı |
|    | 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
|    | Pro | Gly | Gln | Ala | Val | Pro | Ala | Gly | Ser | His | Val | Arg | Leu | Asn | Leu | Glr |
| 10 |     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
|    | Thr | Gly | Glu | Arg | Glu | Ala | Lys | Leu | Gln | Tyr | Glu | Asp | Lys | Phe | Arg | Ası |
|    |     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
|    | Asn | Leu | Lys | Gly | Lys | Arg | Leu | Asp | Ile | Asn | Thr | Asn | Thr | Tyr | Thr | Ser |
|    |     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
| 15 | Gln | Asp | Leu | Lys | Ser | Ala | Leu | Ala | Lys | Phe | Lys | Glu | Gly | Ala | Glu | Met |
|    |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
|    | Glu | Ser | Ser | Lys | Glu | Asp | Lys | Ala | Arg | Gln | Ala | Glu | Val | Lys | Arg | Let |
|    | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
|    | Phe | Arg | Pro | Ile | Glu | Glu | Leu | Lys | Lys | Asp | Phe | Asp | Glu | Leu | Asn | Va] |
| 20 |     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
|    | Val | Ile | Glu | Thr | Asp | Met | Gln | Ile | Met | Val | Arg | Leu | Ile | Asn | Lys | Phe |
|    |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
|    | Asn | Ser | Ser | Ser | Ser | Ser | Leu | Glu | Glu | Lys | Ile | Ala | Ala | Leu | Phe | Asp |
|    |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
| 25 | Leu | Glu | Tyr | Tyr | Val | His | Gln | Met | Asp | Asn | Ala | Gln | Asp | Leu | Leu | Ser |

|    |     | 210 |     |     |     |     | 215 |      |     |     |     | 220 |     |     |     |     |
|----|-----|-----|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Phe | Gly | Gly | Leu | Gln | Val | Val | Ile  | Asn | Gly | Leu | Asn | Ser | Thr | Glu | Pro |
|    | 225 |     |     |     |     | 230 |     |      |     |     | 235 |     |     |     |     | 240 |
|    | Leu | Val | Lys | Glu | Tyr | Ala | Ala | Phe  | Val | Leu | Gly | Ala | Ala | Phe | Ser | Ser |
| 5  |     |     |     |     | 245 |     |     |      |     | 250 |     |     |     |     | 255 |     |
|    | Asn | Pro | Lys | Val | Gln | Val | Glu | Ala  | Ile | Glu | Gly | Gly | Ala | Leu | Gln | Lys |
|    |     |     |     | 260 |     |     |     |      | 265 |     |     |     |     | 270 |     |     |
|    | Leu | Leu | Val | Ile | Leu | Ala | Thr | Glu  | Gln | Pro | Leu | Thr | Ala | Lys | Lys | Lys |
|    |     |     | 275 |     |     |     |     | 280  |     |     |     |     | 285 |     |     |     |
| 10 | Val | Leu | Phe | Ala | Leu | Cys | Ser | Leu  | Leu | Arg | His | Phe | Pro | Tyr | Ala | Glr |
|    |     | 290 |     |     |     |     | 295 |      |     |     |     | 300 |     |     |     |     |
|    | Arg | Gln | Phe | Leu | Lys | Leu | Gly | Gly  | Leu | Gln | Val | Leu | Arg | Thr | Leu | Val |
|    | 305 |     |     |     |     | 310 |     |      |     |     | 315 |     |     |     |     | 320 |
|    | Gln | Glu | Lys | Gly | Thr | Glu | Val | Leu  | Ala | Val | Arg | Val | Val | Thr | Leu | Let |
| 15 |     |     |     |     | 325 |     |     |      |     | 330 |     |     |     |     | 335 |     |
|    | Tyr | Asp | Leu | Val | Thr | Glu | Lys | М́еt | Phe | Ala | Glu | Glu | Glu | Ala | Glu | Let |
|    |     |     |     | 340 |     |     |     |      | 345 |     |     |     |     | 350 |     |     |
|    | Thr | Gln | Glu | Met | Ser | Pro | Glu | Lys  | Leu | Gln | Gln | Tyr | Arg | Gln | Val | His |
|    |     |     | 355 |     |     |     |     | 360  |     |     |     |     | 365 |     |     |     |
| 20 | Leu | Leu | Pro | Gly | Leu | Trp | Glu | Gln  | Gly | Trp | Cys | Glu | Ile | Thr | Ala | His |
|    |     | 370 |     |     |     |     | 375 |      |     |     |     | 380 |     |     |     |     |
|    | Leu | Leu | Ala | Leu | Pro | Glu | His | Asp  | Ala | Arg | Glu | Lys | Val | Leu | Gln | Thi |
|    | 385 |     |     |     |     | 390 |     |      |     |     | 395 |     |     |     |     | 400 |
|    | Leu | Gly | Val | Leu | Leu | Thr | Thr | Cys  | Arg | Asp | Arg | Tyr | Arg | Gln | Asp | Pro |
| 25 |     |     |     |     | 405 |     |     |      |     | 410 |     |     |     |     | 415 |     |

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Gln Leu Gly Arg Thr Leu Ala Ser Leu Gln Ala Glu Tyr Gln Val Leu Ala Ser Leu Glu Leu Gln Asp Gly Glu Asp Glu Gly Tyr Phe Gln Glu Leu Leu Gly Ser Val Asn Ser Leu Leu Lys Glu Leu Arg <210> 4 <211> 647 <212> PRT <213> Homo sapiens <400> 4 Met Ala Ser Leu Val Ser Leu Glu Leu Gly Leu Leu Leu Ala Val Leu Val Val Thr Ala Thr Ala Ser Pro Pro Ala Gly Leu Leu Ser Leu Leu Thr Ser Gly Gln Gly Ala Leu Asp Gln Glu Ala Leu Gly Gly Leu Leu Asn Thr Leu Ala Asp Arg Val His Cys Thr Asn Gly Pro Cys Gly Lys Cys Leu Ser Val Glu Asp Ala Leu Gly Leu Gly Glu Pro Glu Gly Ser Gly Leu Pro Pro Gly Pro Val Leu Glu Ala Arg Tyr Val Ala Arg Leu Ser Ala Ala Ala Val Leu Tyr Leu Ser Asn Pro Glu Gly Thr Cys Glu

|     |     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|     | Asp | Thr | Arg | Ala | Gly | Leu | Trp | Ala | Ser | His | Ala | Asp | His | Leu | Leu | Ala |
|     |     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
|     | Leu | Leu | Glu | Ser | Pro | Lys | Ala | Leu | Thr | Pro | Gly | Leu | Ser | Trp | Leu | Leu |
| 5   |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
|     | Gln | Arg | Met | Gln | Ala | Arg | Ala | Ala | Gly | Gln | Thr | Pro | Lys | Thr | Ala | Cys |
|     | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
|     | Val | Asp | Ile | Pro | Gln | Leu | Leu | Glu | Glu | Ala | Val | Gly | Ala | Gly | Ala | Pro |
|     |     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
| 10  | Gly | Ser | Ala | Gly | Gly | Val | Leu | Ala | Ala | Leu | Leu | Asp | His | Val | Arg | Ser |
|     |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
|     | Gly | Ser | Суз | Phe | His | Ala | Leu | Pro | Ser | Pro | Gln | Tyr | Phe | Val | Asp | Phe |
|     |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
|     | Val | Phe | Gln | Gln | His | Ser | Ser | Glu | Val | Pro | Met | Thr | Leu | Ala | Glu | Leu |
| 15  |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
|     | Ser | Ala | Leu | Met | Gln | Arg | Leu | Gly | Val | Gly | Arg | Glu | Ala | His | Ser | Asp |
|     | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
|     | His | Ser | His | Arg | His | Arg | Gly | Ala | Ser | Ser | Arg | Asp | Pro | Val | Pro | Leu |
|     |     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |
| 20  | Ile | Ser | Ser | Ser | Asn | Ser | Ser | Ser | Val | Trp | Asp | Thr | Val | Cys | Leu | Ser |
|     |     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |
|     | Ala | Arg | Asp | Val | Met | Ala | Ala | Tyr | Gly | Leu | Ser | Glu | Gln | Ala | Gly | Val |
|     |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |
|     | Thr | Pro | Glu | Ala | Trp | Ala | Gln | Leu | Ser | Pro | Ala | Leu | Leu | Gln | Gln | Gln |
| 2.5 |     | 290 |     |     |     |     | 205 |     |     |     |     | 300 |     |     |     |     |

|    | Leu | Ser | Gly | Ala | Cys | Thr | ser | Gln | Ser | Arg | Pro | Pro | Val | Gln | Asp | Gln |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |
|    | Leu | Ser | Gln | Ser | Glu | Arg | Tyr | Leu | Tyr | Gly | Ser | Leu | Ala | Thr | Leu | Leu |
|    |     |     |     |     | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |
| 5  | Ile | Cys | Leu | Cys | Ala | Val | Phe | Gly | Leu | Leu | Leu | Leu | Thr | Cys | Thr | Gly |
|    |     |     |     | 340 |     |     |     |     | 345 |     |     |     |     | 350 |     |     |
|    | Cys | Arg | Gly | Val | Ala | His | Tyr | Ile | Leu | Gln | Thr | Phe | Leu | Ser | Leu | Ala |
|    |     |     | 355 |     |     |     |     | 360 |     |     |     |     | 365 |     |     |     |
|    | Val | Gly | Ala | Leu | Thr | Gly | Asp | Ala | Val | Leu | His | Leu | Thr | Pro | Lys | Val |
| 10 |     | 370 |     |     |     |     | 375 |     |     |     |     | 380 |     |     | •   |     |
|    | Leu | Gly | Leu | His | Thr | His | Ser | Glu | Glu | Gly | Leu | Ser | Pro | Gln | Pro | Thr |
|    | 385 |     | •   |     |     | 390 |     |     |     |     | 395 |     |     |     |     | 400 |
|    | Trp | Arg | Leu | Leu | Ala | Met | Leu | Ala | Gly | Leu | Tyr | Ala | Phe | Phe | Leu | Phe |
|    |     |     |     |     | 405 |     |     |     |     | 410 |     |     |     |     | 415 |     |
| 15 | Glu | Asn | Leu | Phe | Asn | Leu | Leu | Leu | Pro | Arg | Asp | Pro | Glu | Asp | Leu | Glu |
|    |     |     |     | 420 |     |     |     |     | 425 |     |     |     |     | 430 |     |     |
|    | Asp | Gly | Pro | Cys | Gly | His | Ser | Ser | His | Ser | His | Gly | Gly | His | Ser | His |
|    |     |     | 435 |     |     |     |     | 440 |     |     |     |     | 445 |     |     |     |
|    | Gly | Val | Ser | Leu | Gln | Leu | Ala | Pro | Ser | Glu | Leu | Arg | Gln | Pro | Lys | Pro |
| 20 |     | 450 |     |     |     |     | 455 |     |     |     |     | 460 |     |     |     |     |
|    | Pro | His | Glu | Gly | Ser | Arg | Ala | Asp | Leu | Val | Ala | Glu | Glu | Ser | Pro | Glu |
|    | 465 |     |     |     |     | 470 |     |     |     |     | 475 |     |     |     |     | 480 |
|    | Leu | Leu | Asn | Pro | Glu | Pro | Arg | Arg | Leu | Ser | Pro | Glu | Leu | Arg | Leu | Leu |
|    |     |     |     |     | 485 |     |     |     |     | 490 | 4   |     |     |     | 495 |     |
| 25 | Pro | Tyr | Met | Ile | Thr | Leu | Gly | Asp | Ala | Val | His | Asn | Phe | Ala | Asp | Gly |

|    |     |       |       | 500   |     |     |     |     | 505 |     |     |     |     | 510 |     |     |
|----|-----|-------|-------|-------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Leu | Ala   | Val   | Gly   | Ala | Ala | Phe | Ala | Ser | Ser | Trp | Lys | Thr | Gly | Leu | Ala |
|    |     |       | 515   |       |     |     |     | 520 |     |     |     |     | 525 |     |     |     |
|    | Thr | Ser   | Leu   | Ala   | Val | Phe | Cys | His | Glu | Leu | Pro | His | Glu | Leu | Gly | Asp |
| 5  |     | 530   |       |       |     |     | 535 |     |     |     |     | 540 |     |     |     |     |
|    | Phe | Ala   | Ala   | Leu   | Leu | His | Ala | Gly | Leu | Ser | Val | Arg | Gln | Ala | Leu | Let |
|    | 545 |       |       |       |     | 550 |     |     |     |     | 555 |     |     |     |     | 560 |
|    | Leu | Asn   | Leu   | Ala   | Ser | Ala | Leu | Thr | Ala | Phe | Ala | Gly | Leu | Tyr | Val | Ala |
|    |     |       |       |       | 565 |     |     |     |     | 570 |     |     |     |     | 575 |     |
| 10 | Leu | Ala   | Val   | Gly   | Val | Ser | Glu | Glu | Ser | Glu | Ala | Trp | Ile | Leu | Ala | Val |
|    |     |       |       | 580   |     |     |     |     | 585 |     |     |     |     | 590 |     |     |
|    | Ala | Thr   | Gly   | Leu   | Phe | Leu | Tyr | Val | Ala | Leu | Cys | Asp | Met | Leu | Pro | Ala |
|    | •   |       | 595   |       |     |     |     | 600 |     |     |     |     | 605 |     |     |     |
|    | Met | Leu   | Lys   | Val   | Arg | Asp | Pro | Arg | Pro | Trp | Leu | Leu | Phe | Leu | Leu | His |
| 15 |     | 610   |       |       |     |     | 615 |     |     |     |     | 620 |     |     |     |     |
|    | Asn | Val   | Gly   | Leu   | Leu | Gly | Gly | Trp | Thr | Val | Leu | Leu | Leu | Leu | Ser | Leu |
|    | 625 |       |       |       |     | 630 |     |     |     |     | 635 |     |     |     |     | 640 |
|    | Tyr | Glu   | Asp   | Asp   | Ile | Thr | Phe |     |     |     |     |     |     |     |     |     |
|    |     |       |       |       | 645 |     |     |     |     |     |     |     |     |     |     |     |
| 20 |     |       |       |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <21 | 0> 5  |       |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <21 | 1> 44 | 16    |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <21 | 2> PI | RT    |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <21 | 3> но | omo : | sapie | ens |     |     |     |     |     |     |     |     |     |     |     |
| 25 | <40 | 0> 5  |       |       |     |     |     |     |     |     |     |     |     |     |     |     |

|    | Met | Leu | His | Pro | Glu | Thr | Ser | Pro  | Gly  | Arg  | Gly | His | Leu | Leu | Ala  | Va. |
|----|-----|-----|-----|-----|-----|-----|-----|------|------|------|-----|-----|-----|-----|------|-----|
|    | 1   |     |     |     | 5   |     |     |      |      | 10   |     |     |     |     | 15   |     |
|    | Leu | Leu | Ala | Leu | Leu | Gly | Thr | Ala  | Trp  | Ala  | Glu | Val | Trp | Pro | Pro  | Glr |
|    |     |     |     | 20  |     |     |     |      | 25   |      |     |     |     | 30  |      |     |
| 5  | Leu | Gln | Glu | Gln | Ala | Pro | Met | Ala  | Gly  | Ala  | Leu | Asn | Arg | Lys | Glu  | Ser |
|    |     |     | 35  |     |     |     |     | 40   |      |      |     |     | 45  |     |      |     |
|    | Phe | Leu | Leu | Leu | Ser | Leu | His | Asn  | Arg  | Leu  | Arg | Ser | Trp | Val | Gln  | Pro |
|    |     | 50  |     |     |     |     | 55  |      |      |      |     | 60  |     |     |      |     |
|    | Pro | Ala | Ala | Asp | Met | Arg | Arg | Leu  | Asp  | Trp  | Ser | Asp | Ser | Leu | Ala  | Glr |
| 10 | 65  |     |     |     |     | 70  |     |      |      |      | 75  |     | •   |     |      | 80  |
|    | Leu | Ala | Gln | Ala | Arg | Ala | Ala | Leu  | Cys  | Gly  | Ile | Pro | Thr | Pro | Ser  | Ler |
|    |     |     |     |     | 85  |     |     |      |      | 90   |     | •   |     |     | 95   |     |
|    | Ala | Ser | Gly | Leu | Trp | Arg | Thr | Leu  | Gln  | Val  | Gly | Trp | Asn | Met | Gln  | Leu |
|    |     |     |     | 100 |     |     |     |      | 105  |      |     |     |     | 110 |      |     |
| 15 | Leu | Pro | Ala | Gly | Leu | Ala | Ser | Phe  | Val  | Glu  | Val | Val | Ser | Leu | Trp  | Phe |
|    |     |     | 115 |     |     |     |     | 120  |      |      |     |     | 125 |     |      |     |
|    | Ala | Glu | Gly | Gln | Arg | Tyr | Ser | His  | Ala  | Ala  | Gly | Glu | Cys | Ala | Arg  | Asn |
|    |     | 130 |     |     |     |     | 135 |      |      |      |     | 140 |     |     |      |     |
|    | Ala | Thr | Суѕ | Thr | His | Tyr | Thr | Gln  | Leu  | Val  | Trp | Ala | Thr | Ser | Ser  | Gln |
| 20 | 145 |     |     |     |     | 150 |     |      |      |      | 155 |     |     |     |      | 160 |
|    | Leu | Gly | Cys | Gly | Arg | His | Leu | Cys  | Ser  | Ala  | Gly | Gln | Ala | Ala | Ile  | Glu |
|    |     |     |     |     | 165 |     |     |      |      | 170  |     |     |     |     | 175  |     |
|    | Ala | Phe | Val | Cys | Ala | Tyr | Ser | Pro  | Gly  | Gly  | Asn | Trp | Glu | Val | Asn  | Gly |
|    |     |     |     | 180 |     |     |     |      | 185  |      |     |     |     | 190 |      |     |
| 25 | Lvs | Thr | Tle | Tle | Pro | Tur | Lve | Tare | G1 v | 71 a | Пrr | Cur | Com | T   | C++0 | mb~ |

|    |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Ala | Ser | Val | Ser | Gly | Cys | Phe | Lys | Ala | Trp | Asp | His | Ala | Gly | Gly | Leu |
|    |     | 210 |     |     |     |     | 215 |     |     |     | ٥   | 220 |     |     |     |     |
|    | Cys | Glu | Val | Pro | Arg | Asn | Pro | Cys | Arg | Met | Ser | Cys | Gln | Asn | His | Gly |
| 5  | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
|    | Arg | Leu | Asn | Ile | Ser | Thr | Cys | His | Cys | His | Cys | Pro | Pro | Gly | Tyr | Thr |
|    |     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |
|    | Gly | Arg | Tyr | Суѕ | Gln | Val | Arg | Cys | Ser | Leu | Gln | Cys | Val | His | Gly | Arg |
|    |     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |
| 10 | Phe | Arġ | Glu | Glu | Glu | Cys | Ser | Суз | Val | Cys | Asp | Ile | Gly | Tyr | Gly | Gly |
|    |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |
|    | Ala | Gln | Cys | Ala | Thr | Lys | Val | His | Phe | Pro | Phe | His | Thr | Cys | Asp | Leu |
|    |     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |
|    | Arg | Ile | Asp | Gly | Asp | Cys | Phe | Met | Val | Ser | Ser | Glu | Ala | Asp | Thr | Tyr |
| 15 | 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |
|    | Tyr | Arg | Ala | Arg | Met | Lys | Cys | Gln | Arg | Lys | Gly | Gly | Val | Leu | Ala | Gln |
|    |     |     |     |     | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |
|    | Ile | Lys | Ser | Gln | Lys | Val | Gln | Asp | Ile | Leu | Ala | Phe | Tyr | Leu | Gly | Arg |
|    |     |     |     | 340 |     |     |     |     | 345 |     |     |     |     | 350 |     |     |
| 20 | Leu | Glu | Thr | Thr | Asn | Glu | Val | Ile | Asp | Ser | Asp | Phe | Glu | Thr | Arg | Asn |
|    |     |     | 355 |     |     |     |     | 360 |     |     |     |     | 365 |     |     |     |
|    | Phe | Trp | Ile | Gly | Leu | Thr | Tyr | Lys | Thr | Ala | Lys | Asp | Ser | Phe | Arg | Trp |
|    |     | 370 |     |     |     |     | 375 |     |     |     |     | 380 |     |     |     |     |
|    | Ala | Thr | Gly | Glu | His | Gln | Ala | Phe | Thr | Ser | Phe | Ala | Phe | Gly | Gln | Pro |
| 25 | 385 |     |     |     |     | 390 | ŕ   |     |     |     | 395 |     |     |     |     | 400 |

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Asp Asn His Gly Phe Gly Asn Cys Val Glu Leu Gln Ala Ser Ala Ala Phe Asn Trp Asn Asn Gln Arg Cys Lys Thr Arg Asn Arg Tyr Ile Cys Gln Phe Ala Gln Glu His Ile Ser Arg Trp Gly Pro Gly Ser <210> 6 <211> 197 <212> PRT <213> Homo sapiens <400> 6 Met Pro Pro Ala Gly Leu Arg Arg Ala Ala Pro Leu Thr Ala Ile Ala Leu Leu Val Leu Gly Ala Pro Leu Val Leu Ala Gly Glu Asp Cys Leu Trp Tyr Leu Asp Arg Asn Gly Ser Trp His Pro Gly Phe Asn Cys Glu Phe Phe Thr Phe Cys Cys Gly Thr Cys Tyr His Arg Tyr Cys Cys Arg Asp Leu Thr Leu Leu Ile Thr Glu Arg Gln Gln Lys His Cys Leu Ala Phe Ser Pro Lys Thr Ile Ala Gly Ile Ala Ser Ala Val Ile Leu Phe Val Ala Val Val Ala Thr Thr Ile Cys Cys Phe Leu Cys Ser Cys Cys

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|    |         |       | 100  |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
|----|---------|-------|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Tyr Leu | Tyr   | Arg  | Arg | Arg | Gln | Gln | Leu | Gln | Ser | Pro | Phe | Glu | Gly | Gln |
|    |         | 115   |      |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
|    | Glu Ile | Pro   | Met  | Thr | Gly | Ile | Pro | Val | Gln | Pro | Val | Tyr | Pro | Tyr | Pro |
| 5  | 130     |       |      |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
|    | Gln Asp | Pro   | Lys  | Ala | Gly | Pro | Ala | Pro | Pro | Gln | Pro | Gly | Phe | Ile | Tyr |
|    | 145     |       |      |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
|    | Pro Pro | Ser   | Gly  | Pro | Ala | Pro | Gln | Tyr | Pro | Leu | Tyr | Pro | Ala | Gly | Pro |
|    |         |       |      | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
| 10 | Pro Val | Tyr   | Asn  | Pro | Ala | Ala | Pro | Pro | Pro | Tyr | Met | Pro | Pro | Gln | Pro |
|    |         |       | 180  |     |     |     | •   | 185 |     |     |     |     | 190 |     |     |
|    | Ser Tyr | Pro   | Gly  | Ala |     |     |     |     |     |     |     |     |     |     |     |
|    |         | 195   |      |     |     |     |     |     |     |     |     |     |     |     |     |
|    |         |       |      |     |     |     |     |     |     |     |     |     | •   |     |     |
| 15 | <210> 7 |       |      |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <211> 5 | 40    |      |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <212> P | RT    |      |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <213> H | omo s | sapi | ens |     |     |     |     |     |     |     |     |     |     |     |
|    | <400> 7 |       |      |     |     |     |     |     |     |     |     |     |     |     |     |
| 20 | Met Ala | Thr   | Ser  | Gly | Ala | Ala | Ser | Ala | Glu | Leu | Val | Ile | Gly | Trp | Cys |
|    | 1       |       |      | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
|    | Ile Phe | Gly   | Leu  | Leu | Leu | Leu | Ala | Ile | Leu | Ala | Phe | Суз | Trp | Ile | Tyr |
|    |         |       | 20   |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
|    | Val Arg | Lys   | Tyr  | Gln | Ser | Arg | Arg | Glu | Ser | Glu | Val | Val | Ser | Thr | Ile |
| 25 |         | 35    |      |     |     |     | 40  |     |     |     |     | 45  |     |     |     |

|    | Thr | Ala | Ile | Phe | Ser | Leu | Ala | Ile | Ala | Leu | Ile | Thr | Ser | Ala | Leu | Leu |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    |     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
|    | Pro | Val | Asp | Ile | Phe | Leu | Val | Ser | Tyr | Met | Lys | Asn | Gln | Asn | Gly | Thr |
|    | 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
| 5  | Phe | Lys | Asp | Trp | Ala | Asn | Ala | Asn | Val | Ser | Arg | Gln | Ile | Glu | Asp | Thr |
|    |     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
|    | Val | Leu | Tyr | Gly | Tyr | Tyr | Thr | Leu | Tyr | Ser | Val | Ile | Leu | Phe | Cys | Val |
|    |     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
|    | Phe | Phe | Trp | Ile | Pro | Phe | Val | Tyr | Phe | Tyr | Tyr | Glu | Glù | Lys | Asp | Asp |
| LO |     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
|    | Asp | Asp | Thr | Ser | Lys | Cys | Thr | Gln | Ile | Lys | Thr | Ala | Leu | Lys | Tyr | Thr |
|    |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
|    | Leu | Gly | Phe | Val | Val | Ile | Суѕ | Ala | Leu | Leu | Leu | Leu | Val | Gly | Ala | Phe |
|    | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
| 15 | Val | Pro | Leu | Asn | Val | Pro | Asn | Asn | Lys | Asn | Ser | Thr | Glu | Trp | Glu | Lys |
|    |     |     |     | •   | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
|    | Val | Lys | Ser | Leu | Phe | Glu | Glu | Leu | Gly | Ser | Ser | His | Gly | Leu | Ala | Ala |
|    |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
|    | Leu | Ser | Phe | Ser | Ile | Ser | Ser | Leu | Thr | Leu | Ile | Gly | Met | Leu | Ala | Ala |
| 20 |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
|    | Ile | Thr | Tyr | Thr | Ala | Tyr | Gly | Met | Ser | Ala | Leu | Pro | Leu | Asn | Leu | Ile |
|    |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
|    | Lys | Gly | Thr | Arg | Ser | Ala | Ala | Tyr | Glu | Arg | Leu | Glu | Asn | Thr | Glu | Asp |
|    | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
| 25 | Ile | Glu | Glu | Val | Glu | Gln | His | Ile | Gln | Thr | Ile | Lvs | Ser | Lvs | Ser | Lvs |

|    |     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255         |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------------|-----|
|    | Asp | Gly | Arg | Pro | Leu | Pro | Ala | Arg | Asp | Lys | Arg | Ala | Ĺeu | Lys | Gln         | Phe |
|    |     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |             |     |
|    | Glu | Glu | Arg | Leu | Arg | Thr | Leu | Lys | Lys | Arg | Glu | Arg | His | Leu | <b>Gl</b> u | Phe |
| 5  |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |             |     |
|    | Ile | Glu | Asn | Ser | Trp | Trp | Thr | Lys | Phe | Cys | Gly | Ala | Leu | Arg | Pro         | Let |
|    |     | 290 |     |     |     |     | 295 |     |     |     | ,   | 300 |     |     |             |     |
|    | Lys | Ile | Val | Trp | Gly | Ile | Phe | Phe | Ile | Leu | Val | Ala | Leu | Leu | Phe         | ۷al |
|    | 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |             | 320 |
| 10 | Ile | Ser | Leu | Phe | Leu | Ser | Asn | Leu | Asp | Lys | Ala | Leu | His | Ser | Ala         | Gl  |
|    |     |     |     |     | 325 |     |     |     |     | 330 |     |     |     |     | 335         |     |
|    | Ile | Asp | Ser | Gly | Phe | Ile | Ile | Phe | Gly | Ala | Asn | Leu | Ser | Asn | Pro         | Let |
|    |     |     |     | 340 |     |     |     |     | 345 |     |     |     |     | 350 |             |     |
|    | Asn | Met | Leu | Leu | Pro | Leu | Leu | Gln | Thr | Val | Phe | Pro | Leu | Asp | Tyr         | Ile |
| 15 |     |     | 355 |     |     |     |     | 360 |     |     |     |     | 365 |     |             |     |
|    | Leu | Ile | Thr | Ile | Ile | Ile | Met | Tyr | Phe | Ile | Phe | Thr | Ser | Met | Ala         | Gly |
|    |     | 370 |     |     |     |     | 375 |     |     |     |     | 380 |     |     |             |     |
|    | Ile | Arg | Asn | Ile | Gly | Ile | Trp | Phe | Phe | Trp | Ile | Arg | Leu | Tyr | Lys         | Ile |
|    | 385 |     |     |     |     | 390 |     |     |     |     | 395 |     |     |     |             | 400 |
| 20 | Arg | Arg | Gly | Arg | Thr | Arg | Pro | Gln | Ala | Leu | Leu | Phe | Leu | Cys | Met         | Ile |
|    |     |     |     |     | 405 |     |     |     |     | 410 |     |     |     |     | 415         |     |
|    | Leu | Leu | Leu | Ile | Val | Leu | His | Thr | Ser | Tyr | Met | Ile | Tyr | Ser | Leu         | Ala |
|    |     |     |     | 420 |     |     |     |     | 425 |     |     |     |     | 430 |             |     |
|    | Pro | Gln | Tyr | Val | Met | Tyr | Gly | Ser | Gln | Asn | Tyr | Leu | Ile | Glu | Thr         | Asn |
| 25 |     |     | 435 |     |     |     |     | 440 |     |     |     |     | 445 |     |             |     |

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Ile Thr Ser Asp Asn His Lys Gly Asn Ser Thr Leu Ser Val Pro Lys Arg Cys Asp Ala Asp Ala Pro Glu Asp Gln Cys Thr Val Thr Arg Thr Tyr Leu Phe Leu His Lys Phe Trp Phe Phe Ser Ala Ala Tyr Tyr Phe Gly Asn Trp Ala Phe Leu Gly Val Phe Leu Ile Gly Leu Ile Val Ser Cys Cys Lys Gly Lys Lys Ser Val Ile Glu Gly Val Asp Glu Asp Ser Asp Ile Ser Asp Asp Glu Pro Ser Val Tyr Ser Ala <210> 8 <211> 442 <212> PRT <213> Homo sapiens <400> 8 Met Ala Leu Pro Ser Arg Ile Leu Leu Trp Lys Leu Val Leu Leu Gln Ser Ser Ala Val Leu Leu His Ser Gly Ser Ser Val Pro Ala Ala Ala Gly Ser Ser Val Val Ser Glu Ser Ala Val Ser Trp Glu Ala Gly Ala Arg Ala Val Leu Arg Cys Gln Ser Pro Arg Met Val Trp Thr Gln Asp

|    |     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Arg | Leu | His | Asp | Arg | Gln | Arg | Val | Leu | His | Trp | Asp | Leu | Arg | Gly | Pro |
|    | 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
|    | Gly | Gly | Gly | Pro | Ala | Arg | Arg | Leu | Leu | Asp | Leu | Tyr | Ser | Ala | Gly | Glu |
| 5  |     |     |     |     | 85  |     | ٥   |     |     | 90  |     |     |     |     | 95  |     |
|    | Gln | Arg | Val | Tyr | Glu | Ala | Arg | Asp | Arg | Gly | Arg | Leu | Glu | Leu | Ser | Ala |
|    |     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
|    | Ser | Ala | Phe | Asp | Asp | Gly | Asn | Phe | Ser | Leu | Leu | Ile | Arg | Ala | Val | Glu |
|    |     |     | 115 |     |     |     |     | 120 |     |     | •   |     | 125 | ,   | 5   |     |
| LO | Glu | Thr | Asp | Ala | Gly | Leu | Tyr | Thr | Cys | Asn | Leu | His | His | His | Tyr | Cys |
|    |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
|    | His | Leu | Tyr | Glu | Ser | Leu | Ala | Val | Arg | Leu | Glu | Val | Thr | Asp | Gly | Pro |
|    | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
|    | Pro | Ala | Thr | Pro | Ala | Tyr | Trp | Asp | Gly | Glu | Lys | Glu | Val | Leu | Ala | Val |
| L5 |     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
|    | Ala | Arg | Gly | Ala | Pro | Ala | Leu | Leu | Thr | Cys | Val | Asn | Arg | Gly | His | Val |
|    |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
|    | Trp | Thr | Asp | Arg | His | Val | Glu | Glu | Ala | Gln | Gln | Val | Val | His | Trp | Asp |
|    |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
| 20 | Arg | Gln | Pro | Pro | Gly | Val | Pro | His | Asp | Arg | Ala | Asp | Arg | Leu | Leu | Asp |
|    |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
|    | Leu | Tyr | Ala | Ser | Gly | Glu | Arg | Arg | Ala | Tyr | Gly | Pro | Leu | Phe | Leu | Arg |
|    | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
|    | Asp | Arg | Val | Ala | Val | Gly | Ala | Asp | Ala | Phe | Glu | Arg | Gly | Asp | Phe | Ser |
| 25 |     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |

|    | Leu   | Arg | Ile | Glu  | Pro  | Leu | Glu           | Val  | Ala   | Asp      | Glu | Gly            | Thr  | Tyr | Ser | Суѕ |
|----|-------|-----|-----|------|------|-----|---------------|------|-------|----------|-----|----------------|------|-----|-----|-----|
|    |       |     |     | 260  |      |     |               |      | 265   |          |     |                |      | 270 |     |     |
|    | His   | Leu | His | His  | His  | Tyr | Cys           | Gly. | Leu   | His      | Glu | Arg            | Arg  | Val | Phe | His |
|    |       |     | 275 |      |      |     |               | 280  |       |          |     |                | 285  |     |     |     |
| 5  | Leu   | Thr | Val | Ala  | Glu  | Pro | His           | Ala  | Glu   | Pro      | Pro | Pro            | Ara  | Glv | Ser | Pro |
|    |       | 290 |     |      |      |     | 295           |      |       |          |     | 300            |      |     | ,   |     |
|    |       | 230 |     |      |      |     | 233           |      |       |          |     | 300            |      |     |     | •   |
|    | Gly   | Asn | Gly | Ser  | Ser  | His | Ser           | Gly  | Ala   | Pro      | Gly | Pro            | ⁄Asp | Pro | Thr | Leu |
| -  | 305   |     |     |      |      | 310 |               |      |       |          | 315 |                |      |     |     | 320 |
|    | Ala   | Arg | Gly | His  | Asn  | Val | Ile           | Asn  | Val   | Ile      | Val | Pro            | Glu  | Ser | Arg | Ala |
| 10 |       |     |     |      | 325  |     |               |      |       | 330      |     |                |      |     | 335 |     |
|    | ui a  | Dha | Dha | C1 - | C1-  | ۲   | C3            | m    | **- 1 | <b>.</b> |     | <del>~</del> 1 | _    | _   | _   |     |
|    | ഹ     | Phe | rne | GTII | GIII | ьeu | стХ           | ryr  | vaı   | ьеи      | ATA | Thr            | Leu  | Leu | Leu | Phe |
|    |       |     |     | 340  |      |     |               |      | 345   |          |     |                |      | 350 |     |     |
|    | Ile   | Leu | Leu | Leu  | Val  | Thr | Val           | Leu  | Leu   | Ala      | Ala | Arg            | Arg  | Arg | Arg | Gly |
|    |       |     | 355 |      |      |     |               | 360  |       |          |     |                | 365  |     |     |     |
| 15 | Gly   | Tyr | Glu | Tyr  | Ser  | Asp | Gln           | Lys  | Ser   | Gly      | Lys | Ser            | Lys  | Gly | Lys | Asp |
|    |       | 370 |     |      |      |     | 375           |      |       |          |     | 380            |      |     |     |     |
|    |       |     |     |      |      |     |               |      |       |          |     |                |      |     |     |     |
|    | Val   | Asn | Leu | Ala  | Glu  | Phe | Ala           | Val  | Ala   | Ala      | Gly | Asp            | Gln  | Met | Leu | Tyr |
|    | 385   |     |     |      |      | 390 |               |      |       |          | 395 |                |      |     |     | 400 |
|    | Arg   | Ser | Glu | Asp  | Ile  | Gln | Leu           | Asp  | Tyr   | Lys      | Asn | Asn            | Ile  | Leu | Lys | Glu |
| 20 |       |     |     |      | 405  |     |               |      |       | 410      |     |                |      |     | 415 |     |
|    | Arg   | Ala | Glu | Leu  | Ala  | His | Ser           | Pro  | Leu   | Prò      | Ala | Lys            | Tyr  | Ile | Asp | Leu |
|    |       |     |     | 420  |      |     |               |      | 425   |          |     |                |      | 430 |     |     |
|    | 7\ ~~ | T   | C1  | nh - | 7    | T   | <b>~1</b> · · | 7    | ٥.    | -        |     |                |      |     |     |     |
|    | wsb   | Lys |     | rue  | Arg  | тЛЗ | GIU           |      | cys   | тЛ̂г     |     |                |      |     |     |     |
|    |       |     | 435 |      |      |     |               | 440  |       |          |     |                |      |     |     |     |

|            | <210 | )> 9  |       |      |     |     |     |     |     |     |     |     |     |     | •   |     |
|------------|------|-------|-------|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|            | <211 | L> 26 | 52    |      |     |     |     |     |     |     |     |     |     |     |     |     |
|            | <212 | ?> PF | T?    |      |     |     | 43  |     |     |     |     |     |     |     |     |     |
|            | <213 | 3> Ho | omo s | apie | ens |     | •   |     |     |     |     |     |     |     |     |     |
| 5          | <400 | )> 9  |       |      |     |     |     |     |     |     |     |     |     | •   |     |     |
|            | Met  | Thr   | Pro   | Glu  | Asp | Pro | Glu | Glu | Thr | Gln | Pro | Leu | Leu | Gly | Pro | Pro |
|            | 1    |       |       |      | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
|            | Gly  | Gly   | Ser   | Ala  | Pro | Arg | Gly | Arg | Arg | Val | Phe | Leu | Ala | Ala | Phe | Ala |
|            |      |       |       | 20   |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
| LO         | Ala  | Ala   | Leu   | Gly  | Pro | Leu | Ser | Phe | Gly | Phe | Ala | Leu | Gly | Tyr | Ser | Ser |
|            |      |       | 35    |      |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
|            | Pro  | Ala   | Ile   | Pro  | Ser | Leu | Gln | Arg | Ala | Ala | Pro | Pro | Ala | Pro | Arg | Let |
|            |      | -50   |       |      |     |     | 55  |     |     |     |     | 60  | •   |     |     |     |
|            | Asp  | Asp   | Ala   | Ala  | Ala | Ser | Trp | Phe | Gly | Ala | Val | Val | Thr | Leu | Gly | Ala |
| <b>L</b> 5 | 65   |       |       |      |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
|            | Ala  | Ala   | Gly   | Gly  | Val | Leu | Gly | Gly | Trp | Leu | Val | Asp | Arg | Ala | Gly | Arg |
|            |      |       |       |      | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
|            | Lys  | Leu   | Ser   | Leu  | Leu | Leu | Cys | Ser | Val | Pro | Phe | Val | Ala | Gly | Phe | Ala |
|            |      |       |       | 100  |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
| 20         | Val  | Ile   | Thr   | Ala  | Ala | Gln | Asp | Val | Trp | Met | Leu | Leu | Gly | Gly | Arg | Leu |
|            |      |       | 115   |      |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
|            | Leu  | Thr   | Gly   | Leu  | Ala | Cys | Gly | Val | Ala | Ser | Leu | Val | Ala | Pro | Val | Туг |
|            |      | 130   |       |      |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
|            | Ile  | Ser   | Glu   | Ile  | Ala | Tyr | Pro | Ala | Val | Arg | Gly | Leu | Leu | Gly | Ser | Cys |
| 25         | 145  |       |       |      |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |

|    | Val  | Gln   | Leu   | Met   | Val | Val | Val | Gly | Ile | Leu | Leu | Ala | Tyr | Leu | Ala | Gly |
|----|------|-------|-------|-------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    |      |       |       |       | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
|    | Trp  | Val   | Leu   | Glu   | Trp | Arg | Trp | Leu | Ala | Val | Leu | Gly | Cys | Val | Pro | Pro |
|    |      |       |       | 180   |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
| 5  | Ser  | Leu   | Met   | Leu   | Leu | Leu | Met | Cys | Phe | Met | Pro | Glu | Thr | Pro | Arg | Phe |
|    |      |       | 195   |       |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
|    | Leu  | Leu   | Thr   | Gln   | His | Arg | Arg | Gln | Glu | Ala | Ala | Pro | Gly | Leu | Val | Arg |
|    |      | 210   |       |       |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
|    | Cys  | Gly   | His   | Gly   | Val | Gln | His | Glu | Cys | Leu | Arg | Arg | Leu | Leu | Gln | Ala |
| LO | 225  |       |       |       |     | 230 |     |     |     |     | 235 | •   |     |     |     | 240 |
|    | Asp  | Pro   | Gly   | Trp   | Pro | Trp | Gln | Leu | Leu | Ala | Arg | Gly | His | Leu | Gly | Ala |
|    |      |       |       |       | 245 | •   |     |     |     | 250 |     |     |     |     | 255 |     |
|    | Cys  | Leu   | Суѕ   | Thr   | Ala | Cys |     |     |     |     |     |     |     |     |     |     |
|    |      |       |       | 260   |     |     |     |     |     |     |     |     |     |     |     |     |
| 15 |      |       |       |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <210 | )> 10 | )     |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <211 | i> 15 | 52    |       |     |     |     |     |     |     |     |     |     | •   |     |     |
|    | <212 | 2> PF | RT    |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <213 | 3> Ho | omo s | sapie | ens |     |     |     |     |     |     |     |     |     |     |     |
| 20 | <400 | )> 10 | )     |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | Met  | Arg   | Gly   | Pro   | Gly | His | Pro | Leu | Leu | Leu | Gly | Leu | Leu | Leu | Val | Leu |
|    | 1    |       |       |       | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
|    | Gly  | Ala   | Ala   | Gly   | Arg | Gly | Arg | Gly | Gly | Ala | Glu | Pro | Arg | Glu | Pro | Ala |
|    |      |       |       | 20    |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
| 25 | Asp  | Gly   | Gln   | Ala   | Leu | Leu | Arg | Leu | Val | Val | Glu | Leu | Val | Gln | Glu | Leu |

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Arg Lys His His Ser Ala Glu His Lys Gly Leu Gln Leu Leu Gly Arg Asp Cys Ala Leu Gly Arg Ala Glu Ala Ala Gly Leu Gly Pro Ser Pro Glu Gln Arg Val Glu Ile Val Pro Arg Asp Leu Arg Met Lys Asp Lys Phe Leu Lys His Leu Thr Gly Pro Leu Tyr Phe Ser Pro Lys Cys Ser Lys His Phe His Arg Leu Tyr His Asn Thr Arg Asp Cys Thr Ile Pro Ala Tyr Tyr Lys Arg Cys Ala Arg Leu Leu Thr Arg Leu Ala Val Ser Pro Val Cys Met Glu Asp Lys Gln <210> 11 <211> 1737 <212> DNA <213> Homo sapiens <400> 11 atggcatttt ctgaactcct ggacctcgtg ggtggcctgg gcaggttcca ggttctccag 60 acgatggctc tgatggtctc catcatgtgg ctgtgtaccc agagcatgct ggagaacttc 120

teggeegeeg tgeccageca eegetgetgg geaceeetee tggacaacag caeggeteag 180

gccagcatcc tagggagctt gagtcctgag gccctcctgg ctatttccat cccgccgggc 240

5

10

15

20

25

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<211> 732

<212> DNA

5 <213> Homo sapiens

<400> 12

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10

15

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<211> 1386

<212> DNA

<213> Homo sapiens

25 <400> 13

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10

15

#### 27 /346

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20

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<210> 14

<211> 1944

<212> DNA

<213> Homo sapiens

5 <400> 14

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15

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### 29 /346

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|    | aatctcctgc | tgcccaggga | cccggaggac | ctggaggacg | ggccctgcgg | ccacagcagc | 1320 |
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|    | cagcccaagc | cccccacga  | gggetecege | gcagacctgg | tggcggagga | gagcccggag | 1440 |
| 5  | ctgctgaacc | ctgagcccag | gagactgagc | ccagagttga | ggctactgcc | ctatatgatc | 1500 |
|    | actctgggcg | acgccgtgca | caacttcgcc | gacgggctgg | ccgtgggcgc | cgccttcgcg | 1560 |
|    | tcctcctgga | agaccgggct | ggccacctcg | ctggccgtgt | tctgccacga | gttgccacac | 1620 |
|    | gagctggggg | acttcgccgc | cttgctgcac | gcggggctgt | ccgtgcgcca | agcactgctg | 1680 |
|    | ctgaacctgg | cctccgcgct | cacggccttc | gctggtctct | acgtggcact | cgcggttgga | 1740 |
| 10 | gtcagcgagg | agagcgaggc | ctggatcctg | gcagtggcca | ccggcctgtt | cctctacgta | 1800 |
|    | gcactctgcg | acatgctccc | ggcgatgttg | aaagtacggg | acccgcggcc | ctggctcctc | 1860 |
|    | ttcctgctgc | acaacgtggg | cctgctgggc | ggctggaccg | tcctgctgct | gctgtccctg | 1920 |
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<211> 1341

<212> DNA

<213> Homo sapiens

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25 tggegeacee tgeaagtggg etggaacatg eagetgetge eegegggett ggegteettt 360

### 30 /346

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|    | tgtgctcgca | acgccacctg | cacccactac | acgcagctcg | tgtgggccac | ctcaagccag | 480  |
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|    | gcctactccc | ccggaggcaa | ctgggaggtc | aacgggaaga | caatcatccc | ctataagaag | 600  |
| 5  | ggtgcctggt | gttcgctctg | cacagccagt | gtctcaggct | gcttcaaagc | ctgggaccat | 660  |
|    | gcagggggc  | tctgtgaggt | ccccaggaat | ccttgtcgca | tgagctgcca | gaaccatgga | 720  |
|    | cgtctcaaca | tcagcacctg | ccactgccac | tgtccccctg | gctacacggg | cagatactgc | 780  |
|    | caagtgaggt | gcagcctgca | gtgtgtgcac | ggccggttcc | gggaggagga | gtgctcgtgc | 840  |
|    | gtctgtgaca | tcggctacgg | gggagcccag | tgtgccacca | aggtgcattt | tcccttccac | 900  |
| 10 | acctgtgacc | tgaggatcga | cggagactgc | ttcatggtgt | cttcagaggc | agacacctat | 960  |
|    | tacagagcca | ggatgaaatg | tcagaggaaa | ggcggggtgc | tggcccagat | caagagccag | 1020 |
|    | aaagtgcagg | acatcctcgc | cttctatctg | ggccgcctgg | agaccaccaa | cgaggtgatt | 1080 |
|    | gacagtgact | tcgagaccag | gaacttctgg | atcgggctca | cctacaagac | cgccaaggac | 1140 |
|    | teetteeget | gggccacagg | ggagcaccag | gccttcacca | gttttgcctt | tgggcagcct | 1200 |
| 15 | gacaaccacg | ggtttggcaa | ctgcgtggag | ctgcaggctt | cagctgcctt | caactggaac | 1260 |
|    | aaccagcgct | gcaaaacccg | aaaccgttac | atctgccagt | ttgcccagga | gcacatctcc | 1320 |
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<213> Homo sapiens

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#### 31 /346

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20 <211> 1329

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<212> DNA

<213> Homo sapiens

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## 33 /346

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|----|------------|------------|------------|------------|------------|------------|------|
|    | tggacccagg | accggctgca | cgaccgccag | cgcgtgctcc | actgggacct | gegeggeeee | 240  |
|    | gggggtggcc | ccgcgcggcg | cctgctggaç | ttgtactcgg | cgggcgagca | gcgcgtgtac | 300  |
|    | gaggcgcggg | accgcggccg | cctggagctc | tcggcctcgg | ccttcgacga | cggcaacttc | 360  |
| 5  | tcgctgctca | tccgcgcggt | ggaggagacg | gacgcggggc | tgtacacctg | caacctgcac | 420  |
|    | catcactact | gccacctcta | cgagagcctg | gccgtccgcc | tggaggtcac | cgacggcccc | 480  |
|    | ccggccaccc | ccgcctactg | ggacggcgag | aaggaggtgc | tggcggtggc | gcgcggcgca | 540  |
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|    | gctcaacagg | tggtgcactg | ggaccggcag | ccgcccgggg | tcccgcacga | ccgcgcggac | 660  |
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|    | ccgctggagg | tcgccgacga | gggcacctac | tectgecace | tgcaccacca | ttactgtggc | 840  |
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| .5 | gcgcgcggcc | acaacgtcat | caatgtcatc | gtccccgaga | gccgagccca | cttcttccag | 1020 |
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|    | ctggccgccc | gcaggcgccg | cggaggctac | gaatactcgg | accagaagtc | gggaaagtca | 1140 |
|    | aaggggaagg | atgttaactt | ggcggagttc | gctgtggctg | caggggacca | gatgctttac | 1200 |
|    | aggagtgagg | acatccagct | agattacaaa | aacaacatcc | tgaaggagag | ggcggagctg | 1260 |
| 20 | gcccacagcc | ccctgcctgc | caagtacatc | gacctagaca | aagggttccg | gaaggagaac | 1320 |
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34 /346

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35 /346

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Met Ala Phe Ser Glu Leu

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25 10 15 20

|    | gct | ctg | atg | gtc | tcc         | atc | atg | tgg | ctg | tgt | acc | cag | agc | atg | ctg | gag | 451 |
|----|-----|-----|-----|-----|-------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Ala | Leu | Met | Val | Ser         | Ile | Met | Trp | Leu | Cys | Thr | Gln | Ser | Met | Leu | Glu |     |
|    |     |     | 25  |     |             |     |     | 30  |     |     |     |     | 35  |     |     |     |     |
|    | aac | ttc | tcg | gcc | gcc         | gtg | ccc | agc | cac | cgc | tgc | tgg | gca | ccc | ctc | ctg | 499 |
| 5  | Asn | Phe | Ser | Ala | Ala         | Val | Pro | Ser | His | Arg | Cys | Trp | Ala | Pro | Leu | Leu |     |
|    |     | 40  |     |     |             |     | 45  |     |     |     |     | 50  |     |     |     |     |     |
|    | gac | aac | agc | acg | gct         | cag | gcc | agc | atc | cta | ggg | agc | ttg | agt | cct | gag | 547 |
|    | Asp | Asn | Ser | Thr | Ala         | Gln | Ala | Ser | Ile | Leu | Gly | Ser | Leu | Ser | Pro | Glu |     |
|    | 55  |     |     |     |             | 60  |     |     |     |     | 65  |     |     |     |     | 70  |     |
| 10 | gcc | ctc | ctg | gct | att         | tcc | atc | ccg | ccg | ggc | ccc | aac | cag | agg | ccc | cac | 595 |
|    | Ala | Leu | Leu | Ala | Ile         | Ser | Ile | Pro | Pro | Gly | Pro | Asn | Gln | Arg | Pro | His |     |
|    |     |     |     |     | . <b>75</b> |     |     |     |     | 80  |     |     |     |     | 85  |     |     |
|    | cag | tgc | cgc | cgc | ttc         | cgc | cag | cca | cag | tgg | cag | ctc | ttg | gac | ccc | aat | 643 |
|    | Gln | Cys | Arg | Arg | Phe         | Arg | Gln | Pro | Gln | Trp | Gln | Leu | Leu | Asp | Pro | Asn |     |
| 15 |     |     |     | 90  |             |     |     |     | 95  |     |     |     |     | 100 |     |     |     |
|    | gcc | acg | gcc | acc | agc         | tgg | agc | gag | gcc | gac | acg | gag | ccg | tgt | gtg | gat | 691 |
|    | Ala | Thr | Ala | Thr | Ser         | Trp | Ser | Glu | Ala | Asp | Thr | Glu | Pro | Cys | Val | Asp |     |
|    |     |     | 105 |     |             |     |     | 110 |     |     |     |     | 115 |     |     |     |     |
|    | ggc | tgg | gtc | tat | gac         | cgc | agc | atc | ttc | acc | tcc | aca | atc | gtg | gcc | aag | 739 |
| 20 | Gly | Trp | Val | Tyr | Asp         | Arg | Ser | Ile | Phe | Thr | Ser | Thr | Ile | Val | Ala | Lys |     |
|    |     | 120 |     |     |             |     | 125 |     |     |     |     | 130 |     |     |     |     |     |
|    | tgg | aac | ctc | gtg | tgt         | gac | tct | cat | gct | ctg | aag | ccc | atg | gcc | cag | tcc | 787 |
|    | Trp | Asn | Leu | Val | Cys         | Asp | Ser | His | Ala | Leu | Lys | Pro | Met | Ala | Gln | Ser |     |
|    | 135 |     |     |     |             | 140 |     |     |     |     | 145 |     |     |     |     | 150 |     |
| 25 | atc | tac | ctg | gct | ggg         | att | ctg | gtg | gga | gct | gct | gcg | tgc | ggc | cct | gcc | 835 |

|    | Ile | Tyr | Leu | Ala | Gly | Ile | Leu | Val | Gly | Ala | Ala | Ala | Cys | Gly | Pro | Ala |      |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|    |     |     |     |     | 155 |     |     |     |     | 160 |     |     |     |     | 165 |     |      |
|    | tca | gac | agg | ttt | ggg | cgc | agg | ctg | gtg | cta | acc | tgg | agc | tac | ctt | cag | 883  |
|    | Ser | Asp | Arg | Phe | Gly | Arg | Arg | Leu | Val | Leu | Thr | Trp | Ser | Tyr | Leu | Gln |      |
| 5  |     | •   |     | 170 |     |     |     |     | 175 |     |     | •   |     | 180 |     |     |      |
|    | atg | gct | gtg | atg | ggt | acg | gca | gct | gcc | ttc | gcc | cct | gcc | ttc | ccc | gtg | 931  |
|    | Met | Ala | Val | Met | Gly | Thr | Ala | Ala | Ala | Phe | Ala | Pro | Ala | Phe | Pro | Val |      |
|    |     |     | 185 |     |     |     |     | 190 |     |     |     |     | 195 |     |     |     |      |
|    | tac | tgc | ctg | ttc | cgc | ttc | ctg | ttg | gcc | ttt | gcc | gtg | gca | ggc | gtc | atg | 979  |
| 10 | Tyr | Cys | Leu | Phe | Arg | Phe | Leu | Leu | Ala | Phe | Ala | Val | Ala | Gly | Val | Met |      |
|    |     | 200 |     |     | •   |     | 205 |     |     |     | •   | 210 |     |     |     |     |      |
|    | atg | aac | acg | ggc | act | ctc | cgt | agg | tct | ctg | acc | tgg | cgc | cat | gca | ggg | 1027 |
| •  | Met | Asn | Thr | Gly | Thr | Leu | Arg | Arg | Ser | Leu | Thr | Trp | Arg | His | Ala | Gly |      |
|    | 215 |     |     |     |     | 220 |     |     |     |     | 225 |     |     |     |     | 230 |      |
| 15 | ggg | ctc | cat | gca | ggc | tcc | agg | gct | gaa | cca | ctc | ggt | ctc | ctt | gca | gtg | 1075 |
|    | Gly | Leu | His | Ala | Gly | Ser | Arg | Ala | Glu | Pro | Leu | Gly | Leu | Leu | Ala | Val |      |
|    |     |     |     |     | 235 |     |     |     |     | 240 |     |     |     |     | 245 |     |      |
|    | atg | gag | tgg | acg | gcg | gca | cgg | gcc | cga | ccc | ttg | gtg | atg | acc | ttg | aac | 1123 |
|    | Met | Glu | Trp | Thr | Ala | Ala | Arg | Ala | Arg | Pro | Leu | Val | Met | Thr | Leu | Asn |      |
| 20 |     |     |     | 250 |     |     |     |     | 255 |     |     |     |     | 260 |     |     |      |
|    | tct | ctg | ggc | ttc | agc | ttc | ggc | cat | ggc | ctg | aca | gct | gca | gtg | gcc | tac | 1171 |
|    | Ser | Leu | Gly | Phe | Ser | Phe | Gly | His | Gly | Leu | Thr | Ala | Ala | Val | Ala | Tyr |      |
|    |     |     | 265 |     |     |     |     | 270 |     |     |     |     | 275 |     |     |     |      |
|    | ggt | gtg | cgg | gac | tgg | aca | ctg | ctg | cag | ctg | gtg | gtc | tcg | gtc | ccc | ttc | 1219 |
| 25 | Gly | Val | Arg | Asp | Trp | Thr | Leu | Leu | Gln | Leu | Val | Val | Ser | Val | Pro | Phe |      |

|    |     | 280 |     |     |     |     | 285 |     |     |     |     | 290 |     |     |     |     |      |
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|    | ttc | ctc | tgc | ttt | ttg | tac | tcc | tgg | tgg | ctg | gca | gag | tcg | gca | cga | tgg | 1267 |
|    | Phe | Leu | Cys | Phe | Leu | Tyr | Ser | Trp | Trp | Leu | Ala | Glu | Ser | Ala | Arg | Trp |      |
|    | 295 |     |     |     |     | 300 |     |     |     |     | 305 |     |     |     |     | 310 |      |
| 5  | ctc | ctc | acc | aca | ggc | agg | ctg | gat | tgg | ggc | ctg | cag | gag | ctg | tgg | agg | 1315 |
|    | Leu | Leu | Thr | Thr | Gly | Arg | Leu | Asp | Trp | Gly | Leu | Gln | Glu | Leu | Trp | Arg |      |
|    |     |     |     |     | 315 |     |     |     |     | 320 |     |     |     |     | 325 |     |      |
|    | gtg | gct | gcc | atc | aac | gga | aag | ggg | gca | gtg | cag | gac | acc | ctg | acc | cct | 1363 |
|    | Val | Ala | Ala | Ile | Asn | Gly | Lys | Gly | Ala | Val | Gln | Asp | Thr | Leu | Thr | Pro |      |
| 10 |     |     |     | 330 |     |     |     |     | 335 |     |     |     |     | 340 |     |     |      |
|    | gag | gtc | ttg | ctt | tca | gcc | atg | cgg | gag | gag | ctg | agc | atg | ggc | cag | cct | 1411 |
| ٠  | Glu | Val | Leu | Leu | Ser | Ala | Met | Arg | Glu | Glu | Leu | Ser | Met | Gly | Gln | Pro |      |
|    |     |     | 345 |     |     |     |     | 350 |     |     |     |     | 355 |     |     |     |      |
|    | cct | gcc | agc | ctg | ggc | acc | ctg | ctc | cgc | atg | ccc | gga | ctg | cgc | ttc | cgg | 1459 |
| 15 | Pro | Ala | Ser | Leu | Gly | Thr | Leu | Leu | Arg | Met | Pro | Gly | Leu | Arg | Phe | Arg |      |
|    |     | 360 |     |     |     |     | 365 |     |     |     |     | 370 |     |     |     |     |      |
|    | acc | tgt | atc | tcc | acg | ttg | tgc | tgg | ttc | gcc | ttt | ggc | ttc | acc | ttc | ttc | 1507 |
|    | Thr | Cys | Ile | Ser | Thr | Leu | Cys | Trp | Phe | Ala | Phe | Gly | Phe | Thr | Phe | Phe |      |
| •  | 375 |     |     |     |     | 380 |     |     |     |     | 385 |     |     |     |     | 390 |      |
| 20 | ggc | ctg | gcc | ctg | gac | ctg | cag | gcc | ctg | ggc | agc | aac | atc | ttc | ctg | ctc | 1555 |
|    | Gly | Leu | Ala | Leu | Asp | Leu | Gln | Ala | Leu | Gly | Ser | Asn | Ile | Phe | Leu | Leu |      |
|    |     |     |     |     | 395 |     |     |     |     | 400 |     |     |     |     | 405 |     |      |
|    |     |     |     | att |     |     |     |     |     |     |     |     |     |     |     |     | 1603 |
|    | Gln | Met | Phe | Ile | Gly | Val | Val | Asp |     | Pro | Ala | Lys | Met | Gly | Ala | Leu |      |
| 25 |     |     |     | 410 |     |     |     |     | 415 |     |     |     |     | 420 |     |     |      |

|    | ctg | ctg | ctg | agc | cac | ctg | ggc | cgc | cgc | CCC | acg | ctg | gcc | gca | tcc | ctg | 1651 |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|    | Leu | Leu | Leu | Ser | His | Leu | Gly | Arg | Arg | Pro | Thr | Leu | Ala | Ala | Ser | Leu |      |
|    |     |     | 425 |     |     |     |     | 430 |     |     |     |     | 435 |     |     |     |      |
|    | ttg | ctg | gcg | ggg | ctc | tgc | att | ctg | gcc | aac | acg | ctg | gtg | ccc | cac | gaa | 1699 |
| 5  | Leu | Leu | Ala | Gly | Leu | Cys | Ile | Leu | Ala | Asn | Thr | Leu | Val | Pro | Hĭs | Glu |      |
|    |     | 440 |     |     |     |     | 445 |     |     |     |     | 450 |     |     |     |     |      |
|    | atg | ggg | gct | ctg | cgc | tca | gcc | ctg | gcc | gtg | ctg | ggg | ctg | ggc | ggg | gtg | 1747 |
|    | Met | Gly | Ala | Leu | Arg | Ser | Ala | Leu | Ala | Val | Leu | Gly | Leu | Gly | Gly | Val |      |
|    | 455 |     |     |     |     | 460 |     |     | •   |     | 465 |     |     |     |     | 470 |      |
| 10 | ggg | gct | gcc | ttc | acc | tgc | atc | acc | atc | tac | agc | agc | gag | ctc | ttc | ccc | 1795 |
|    | Gly | Ala | Ala | Phe | Thr | Cys | Ile | Thr | Ile | Tyr | Ser | Ser | Glu | Leu | Phe | Pro |      |
|    |     |     |     |     | 475 |     |     |     |     | 480 |     |     |     |     | 485 |     |      |
|    | act | gtg | ctc | agg | atg | acg | gca | gtg | ggc | ttg | ggc | cag | atg | gca | gcc | cgt | 1843 |
|    | Thr | Val | Leu | Arg | Met | Thr | Ala | Val | Gly | Leu | Gly | Gln | Met | Ala | Ala | Arg |      |
| 15 |     |     |     | 490 |     |     |     |     | 495 |     |     |     |     | 500 |     |     |      |
|    | gga | gga | gcc | atc | ctg | ggg | cct | ctg | gtc | cgg | ctg | ctg | ggt | gtc | cat | ggc | 1891 |
|    | Gly | Gly | Ala | Ile | Leu | Gly | Pro | Leu | Val | Arg | Leu | Leu | Gly | Val | His | Gly |      |
|    |     |     | 505 |     |     |     |     | 510 |     |     |     |     | 515 |     |     |     |      |
|    | ccc | tgg | ctg | ccc | ttg | ctg | gtg | tat | ggg | acg | gtg | cca | gtg | ctg | agt | ggc | 1939 |
| 20 | Pro | Trp | Leu | Pro | Leu | Leu | Val | Tyr | Gly | Thr | Val | Pro | Val | Leu | Ser | Gly |      |
|    |     | 520 |     |     |     |     | 525 |     |     |     |     | 530 |     |     |     |     |      |
|    | ctg | gcc | gca | ctg | ctt | ctg | ccc | gag | acc | cag | agc | ttg | ccg | ctg | ccc | gac | 1987 |
|    | Leu | Ala | Ala | Leu | Leu | Leu | Pro | Glu | Thr | Gln | Ser | Leu | Pro | Leu | Pro | Asp |      |
|    | 535 |     |     |     |     | 540 |     |     |     |     | 545 |     |     |     |     | 550 |      |
| 25 | acc | atc | caa | gat | gtg | cag | aac | cag | gca | gta | aag | aag | gca | aca | cat | ggc | 2035 |

40 /346

Thr Ile Gln Asp Val Gln Asn Gln Ala Val Lys Lys Ala Thr His Gly

555 560 565

acg ctg ggg aac tct gtc cta aaa tcc aca cag ttt tagcctcctg 2081

Thr Leu Gly Asn Ser Val Leu Lys Ser Thr Gln Phe

5 570 575

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|    | aac | tctg  | gtc ( | ccgg  | gcago | cc aa | agac | aaago | c gaa | aaggo | caag | gca | gc a | tg a | gc c | ga tca | 57  |
| 5  |     |       |       |       |       |       |      |       |       |       |      |     | M    | et S | er A | rg Ser |     |
|    |     |       |       |       |       |       |      |       |       |       |      |     |      | 1    |      |        |     |
|    | ccc | ctc   | aat   | ccc   | agc   | caa   | ctc  | cga   | tca   | gtg   | ggc  | tcc | cag  | gat  | gcc  | ctg    | 105 |
|    | Pro | Leu   | Asn   | Pro   | Ser   | Gln   | Leu  | Arg   | Ser   | Val   | Gly  | Ser | Gln  | Asp  | Ala  | Leu    |     |
|    | 5   |       |       |       |       | 10    |      |       |       |       | 15   |     |      |      |      | 20     |     |
| 10 | gcc | ccc   | ttg   | cct   | сса   | cct   | gct  | ccc   | cag   | aat   | ccc  | tcc | acc  | cac  | tct  | tgg    | 153 |
|    | Ala | Pro   | Leu   | Pro   | Pro   | Pro   | Ala  | Pro   | Gln   | Asn   | Pro  | Ser | Thr  | His  | Ser  | Trp    |     |
|    |     |       |       |       | 25    |       |      |       |       | 30    |      |     |      |      | 35   |        |     |
|    | gac | cct   | ttg   | tgt   | gga   | tct   | ctg  | cct   | tgg   | ggc   | ctc  | agc | tgt  | ctt  | ctg  | gct    | 201 |
|    | Asp | Pro   | Leu   | Cys   | Gly   | Ser   | Leu  | Pro   | Trp   | Gly   | Leu  | Ser | Cys  | Leu  | Leu  | Ala    |     |
| 15 |     |       | -     | 40    |       |       |      |       | 45    |       |      |     |      | 50   |      |        |     |
|    | ctg | cag   | cat   | gtc   | ttg   | gtc   | atg  | gct   | tct   | ctg   | ctc  | tgt | gtc  | tcc  | cac  | ctg    | 249 |
|    | Leu | Gln   | His   | Val   | Leu   | Val   | Met  | Ala   | Ser   | Leu   | Leu  | Cys | Val  | Ser  | His  | Leu    |     |
|    |     |       | 55    |       |       |       |      | 60    |       |       |      |     | 65   |      |      |        |     |
|    | ctc | ctg   | ctt   | tgc   | agt   | ctc   | tcc  | cca   | gga   | gga   | ctc  | tct | tac  | tcc  | cct  | tct    | 297 |
| 20 | Leu | Leu   | Leu   | Cys   | Ser   | Leu   | Ser  | Pro   | Gly   | Gly   | Leu  | Ser | Tyr  | Ser  | Pro  | Ser    |     |
|    |     | 70    |       |       |       |       | 75   |       |       |       |      | 80  |      |      |      |        |     |
|    | cag | ctc   | ctg   | gcc   | tcc   | agc   | ttc  | ttt   | tca   | tgt   | ggt  | atg | tct  | acc  | atc  | ctg    | 345 |
|    | Gln | Leu   | Leu   | Ala   | Ser   | Ser   | Phe  | Phe   | Ser   | Cys   | Gly  | Met | Ser  | Thr  | Ile  | Leu    |     |
|    | 85  |       |       |       |       | 90    |      |       |       |       | 95   |     |      |      |      | 100    |     |
| 25 | caa | act   | tgg   | atg   | ggc   | agc   | agg  | ctg   | cct   | ctt   | gtc  | cag | gct  | cca  | tcc  | tta    | 393 |

|    | Gln | Thr | Trp | Met | Gly | Ser | Arg | Leu | Pro | Leu | Val | Gln | Ala | Pro | Ser | Leu |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    |     |     |     |     | 105 |     |     |     |     | 110 |     |     |     |     | 115 |     |     |
|    | gag | ttc | ctt | atc | cct | gct | ctg | gtg | ctg | acc | agc | cag | aag | cta | ccc | cgg | 441 |
|    | Glu | Phe | Leu | Ile | Pro | Ala | Leu | Val | Leu | Thr | Ser | Gln | Lys | Leu | Pro | Arg |     |
| 5  |     |     |     | 120 |     |     |     |     | 125 |     |     |     |     | 130 |     |     |     |
|    | gcc | atc | cag | aca | cct | gga | aac | tcc | tcc | ctc | atg | ctg | cac | ctt | tgt | agg | 489 |
|    | Ala | Ile | Gln | Thr | Pro | Gly | Asn | Ser | Ser | Leu | Met | Leu | His | Leu | Cys | Arg |     |
|    |     |     | 135 |     |     |     |     | 140 |     |     |     |     | 145 |     |     |     |     |
|    | gga | cct | agc | tgc | cat | ggc | ctg | ggg | cac | tgg | aac | act | tct | ctc | cag | gag | 537 |
| 10 | Gly | Pro | Ser | Cys | His | Gly | Leu | Gly | His | Trp | Asn | Thr | Ser | Leu | Gln | Glu |     |
|    |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |     |     |     |     |     |
|    | gtg | tcc | ggg | gca | gtg | gta | gta | tct | ggg | ctg | ctg | cag | ggc | atg | atg | ggg | 585 |
|    | Val | Ser | Gly | Ala | Val | Val | Val | Ser | Gly | Leu | Leu | Gln | Gly | Met | Met | Gly |     |
|    | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |     |     |     | 180 |     |
| 15 | ctg | ctg | ggg | agt | ccc | ggc | cac | gtg | ttc | ccc | cac | tgt | ggg | ccc | ctg | gtg | 633 |
|    | Leu | Leu | Gly | Ser | Pro | Gly | His | Val | Phe | Pro | His | Cys | Gly | Pro | Leu | Val |     |
|    |     |     |     |     | 185 |     |     |     |     | 190 |     |     |     |     | 195 |     |     |
|    | ctg | gct | ccc | agc | ctg | gtt | gtg | gca | ggg | ctc | tct | gcc | cac | agg | gag | gta | 681 |
|    | Leu | Ala | Pro | Ser | Leu | Val | Val | Ala | Gly | Leu | Ser | Ala | His | Arg | Glu | Val |     |
| 20 |     |     |     | 200 |     |     |     |     | 205 |     |     |     |     | 210 |     |     |     |
|    | gcc | cag | ttc | tgc | ttc | aca | cac | tgg | ggg | ttg | gcc | ttg | ctg | tac | gtg | agt | 729 |
|    | Ala | Gln | Phe | Cys | Phe | Thr | His | Trp | Gly | Leu | Ala | Leu | Leu | Tyr | Val | Ser |     |
|    |     |     | 215 |     |     |     |     | 220 |     |     |     |     | 225 |     |     |     |     |
|    | cct | gag | agg | cgt | ggg | atg | gtg | ccc | agt | aaa | ggt | gta | tgg | ggg | gac |     | 774 |
| 25 | Pro | Glu | Arg | Arg | Gly | Met | Val | Pro | Ser | Glv | Glv | Va] | Tro | Glv | Asp |     |     |

230 235 240

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#### 44 /346

| ctcctcctgc | agctttcctc | tgtcatttgg | ataatctcct | tcgcccattg | ttgaaggacg | 2274 |
|------------|------------|------------|------------|------------|------------|------|
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| gggtgcgaag | tgagctctct | ggcctcccct | tctattggaa | tttccactgc | atgctagcta | 2394 |
| gtccttccct | ggtctcccaa | catttgattc | gtcctctgat | gggcatgagt | ctggcattac | 2454 |
| agtgccaagt | gagggagcta | gcaacgttac | ttcatatgaa | agacctagag | atccaagact | 2514 |
| accaggagag | tggggctacg | ctgattcgag | atcgattgaa | gacagaacca | tttgaagaaa | 2574 |
| attecttett | ggaacaattt | atgatagaga | aactgccaga | ggcatgcagc | attggtgatg | 2634 |
| gaaagccctt | tgtcatgaat | ctgcaggatc | tgtatatggc | agtcaccaca | caagaggtcc | 2694 |
| aagtgggaca | gaagcatcaa | ggcgctggag | atcctcatac | ctcaaacagt | gcttccctgc | 2754 |
| aaggaatcga | tagccaatgt | gtaaaccagc | cagaacaact | ggtctcctca | gccccaaccc | 2814 |
| tctcagcacc | tgagaaagag | tecaegggta | cttcaggccc | tctgcagaga | cctcagctgt | 2874 |
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| ctttaggtat | atagggcaag | tcagcaagaa | agcaccacac | actcaggaag | ccttgtctac | 3234 |
| ctttccctag | cgtctctagc | cagccagccc | cagatactcc | tcagagaccc | acttctctct | 3294 |
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45 /346

|    | <221> CDS     |             |            |                  |                  |     |
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| 5  | aggtccctga ct | atg gct co  | c cag agc  | ctg cct tca tct  | agg atg gct cct  | 111 |
|    |               | Met Ala Pr  | o Gln Ser  | Leu Pro Ser Ser  | Arg Met Ala Pro  | •   |
|    |               | 1           | 5          |                  | 10               |     |
|    | ctg ggc atg   | ctg ctt ggg | ctg ctg a  | tg gcc gcc tgc t | tc acc ttc tgc   | 159 |
|    | Leu Gly Met 1 | Leu Leu Gly | Leu Leu M  | et Ala Ala Cys P | he Thr Phe Cys   |     |
| 10 | 15            |             | 20         | 25               |                  |     |
|    | ctc agt cat   | cag aac ctg | aag gag t  | tt gcc ctg acc a | ac cca gag aag   | 207 |
|    | Leu Ser His   | Gln Asn Leu | Lys Glu P  | he Ala Leu Thr A | sn Pro Glu Lys   |     |
|    | 30            | 35          |            | 40               | 45               |     |
|    | agc agc acc   | aaa gaa aca | gag aga a  | aa gaa acc aaa g | JCC gag gag gag  | 255 |
| 15 | Ser Ser Thr   | Lys Glu Thr | Glu Arg I  | ys Glu Thr Lys A | Ala Glu Glu Glu  |     |
|    |               | 50          |            | 55               | 60               |     |
|    | ctg gat gcc   | gaa gtc ctg | gag gtg t  | tc cac ccg acg   | cat gag tgg cag  | 303 |
|    | Leu Asp Ala   | Glu Val Leu | Glu Val H  | Phe His Pro Thr  | His Glu Trp Gln  |     |
|    |               | 65          |            | 70               | 75               |     |
| 20 | gcc ctt cag   | cca ggg cag | gct gtc    | ect gca gga tec  | cac gta cgg ctg  | 351 |
|    | Ala Leu Gln   | Pro Gly Gln | Ala Val    | Pro Ala Gly Ser  | His Val Arg Leu  |     |
|    | 80            |             | 85         |                  | 90               |     |
|    | aat ctt cag   | act ggg gaa | aga gag    | gca aaa ctc caa  | tat gag gac aag  | 399 |
|    | Asn Leu Gln   | Thr Gly Glu | Arg Glu    | Ala Lys Leu Gln  | Tyr Glu Asp Lys  |     |

|    | ttc | cga | aat | aat | ttg | aaa | ggc | aaa | agg | ctg | gat | atc | aac | acc | aac | acc | 447 |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Phe | Arg | Asn | Asn | Leu | Lys | Gly | Lys | Arg | Leu | Asp | Ile | Asn | Thr | Asn | Thr |     |
|    | 110 |     |     |     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |
|    | tac | aca | tct | cag | gat | ctc | aag | agt | gca | ctg | gca | aaa | ttc | aag | gag | ggg | 495 |
| 5  | Tyr | Thr | Ser | Gln | Asp | Leu | Lys | Ser | Ala | Leu | Ala | Lys | Phe | Lys | Glu | Gly |     |
|    |     |     |     |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |
|    | gca | gag | atg | gag | agt | tca | aag | gaa | gac | aag | gca | agg | cag | gct | gag | gta | 543 |
|    | Ala | Glu | Met | Glu | Ser | Ser | Lys | Glu | Asp | Lys | Ala | Arg | Gln | Ala | Glu | Val |     |
|    |     |     |     | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |
| 10 | aag | cgg | ctc | ttc | cgc | ccc | att | gag | gaa | ctg | aag | aaa | gac | ttt | gat | gag | 591 |
|    | Lys | Arg | Leu | Phe | Arg | Pro | Ile | Glu | Glu | Leu | Lys | Lys | Asp | Phe | Asp | Glu |     |
|    |     |     | 160 |     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     |
|    | ctg | aat | gtt | gtc | att | gag | act | gac | atg | cag | atc | atg | gta | cgg | ctg | atc | 639 |
|    | Leu | Asn | Val | Val | Ile | Glu | Thr | Asp | Met | Gln | Ile | Met | Val | Arg | Leu | Ile |     |
| 15 |     | 175 |     |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     |     |
|    | aac | aag | ttc | aat | agt | tcc | agc | tcc | agt | ttg | gaa | gag | aag | att | gct | gcg | 687 |
|    | Asn | Lys | Phe | Asn | Ser | Ser | Ser | Ser | Ser | Leu | Glu | Glu | Lys | Ile | Ala | Ala |     |
|    | 190 |     |     |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |
|    | ctc | ttt | gat | ctt | gaa | tat | tat | gtc | cat | cag | atg | gac | aat | gcg | cag | gac | 735 |
| 20 | Leu | Phe | Asp | Leu | Glu | Tyr | Tyr | Val | His | Gln | Met | Asp | Asn | Ala | Gln | Asp |     |
|    |     |     |     |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |
|    | ctg | ctt | tcc | ttt | ggt | ggt | ctt | caa | gtg | gtg | atc | aat | ggg | ctg | aac | agc | 783 |
|    | Leu | Leu | Ser | Phe | Gly | Gly | Leu | Gln | Val | Val | Ile | Asn | Gly | Leu | Asn | Ser |     |
|    |     |     |     | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |
| 25 | aca | gag | ccc | ctc | gtg | aag | gag | tat | gct | gcg | ttt | gtg | ctg | ggc | gct | gcc | 831 |

|    | Thr | Glu | Pro | Leu | Val | Lys | Glu | Tyr | Ala | Ala | Phe | Val | Leu | Gly | Ala | Ala |      |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|    |     |     | 240 |     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |      |
|    | ttt | tcc | agc | aac | ccc | aag | gtc | cag | gtg | gag | gcc | atc | gaa | ggg | gga | gcc | 879  |
|    | Phe | Ser | Ser | Asn | Pro | Lys | Val | Gln | Val | Glu | Ala | Ile | Glu | Gly | Gly | Ala |      |
| 5  |     | 255 |     |     |     |     | 260 |     |     |     | •   | 265 |     |     |     |     |      |
|    | ctg | cag | aag | ctg | ctg | gtc | atc | ctg | gcc | acg | gag | cag | ccg | ctc | act | gca | 927  |
|    | Leu | Gln | Lys | Leu | Leu | Val | Ile | Leu | Ala | Thr | Glu | Gln | Pro | Leu | Thr | Ala |      |
|    | 270 |     |     |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |      |
|    | aag | aag | aag | gtc | ctg | ttt | gca | ctg | tgc | tcc | ctg | ctg | cgc | cac | ttc | ccc | 975  |
| 10 | Lys | Lys | Lys | Val | Leu | Phe | Ala | Leu | Суз | Ser | Leu | Leu | Arg | His | Phe | Pro |      |
|    |     |     |     |     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |      |
|    | tat | gcc | cag | cgg | cag | ttc | ctg | aag | ctc | ggg | ggg | ctg | cag | gtc | ctg | agg | 1023 |
|    | Tyr | Ala | Gln | Arg | Gln | Phe | Leu | Lys | Leu | Gly | Gly | Leu | Gln | Val | Leu | Arg |      |
|    |     |     |     | 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |     |      |
| 15 | acc | ctg | gtg | cag | gag | aag | ggc | acg | gag | gtg | ctc | gcc | gtg | cgc | gtg | gtc | 1071 |
|    | Thr | Leu | Val | Gln | Glu | Lys | Gly | Thr | Glu | Val | Leu | Ala | Val | Arg | Val | Val |      |
|    |     |     | 320 |     |     |     |     | 325 |     |     |     |     | 330 |     |     |     |      |
|    | aca | ctg | ctc | tac | gac | ctg | gtc | acg | gag | aag | atg | ttc | gcc | gag | gag | gag | 1119 |
|    | Thr | Leu | Leu | Tyr | Asp | Leu | Val | Thr | Glu | Lys | Met | Phe | Ala | Glu | Glu | Glu |      |
| 20 |     | 335 |     |     |     |     | 340 |     |     |     |     | 345 |     |     |     |     |      |
|    | gct | gag | ctg | acc | cag | gag | atg | tcc | cca | gag | aag | ctg | cag | cag | tat | cgc | 1167 |
| •  | Ala | Glu | Leu | Thr | Gln | Glu | Met | Ser | Pro | Glu | Lys | Leu | Gln | Gln | Tyr | Arg |      |
|    | 350 |     |     |     |     | 355 |     |     |     |     | 360 |     |     |     |     | 365 |      |
|    | cag | gta | cac | ctc | ctg | cca | ggc | ctg | tgg | gaa | cag | ggc | tgg | tgc | gag | atc | 1215 |
| 25 | Gln | Val | His | Leu | Leu | Pro | Gly | Leu | Trp | Glu | Gln | Gly | Trp | Cys | Glu | Ile |      |

|    |      |       |       |       | 370   |       |       |       |     | 375   |      |      |       |       | 380   |        |      |
|----|------|-------|-------|-------|-------|-------|-------|-------|-----|-------|------|------|-------|-------|-------|--------|------|
|    | acg  | gcc   | cac   | ctc   | ctg   | gcg   | ctg   | ccc   | gag | cat   | gat  | gcc  | cgt   | gag   | aag   | gtg    | 1263 |
|    | Thr  | Ala   | His   | Leu   | Leu   | Ala   | Leu   | Pro   | Glu | His   | Asp  | Ala  | Arg   | Glu   | Lys   | Val    |      |
|    |      |       |       | 385   |       |       |       |       | 390 |       |      |      |       | 395   |       |        |      |
| 5  | ctg  | cag   | aca   | ctg   | ggc   | gtc   | ctc   | ctg   | acc | acc   | tgc  | cgg  | gac   | cgc   | tac   | cgt    | 1311 |
|    | Leu  | Gln   | Thr   | Leu   | Gly   | Val   | Leu   | Leu   | Thr | Thr   | Cys  | Arg  | Asp   | Arg   | Tyr   | Arg    |      |
|    |      |       | 400   |       |       |       |       | 405   |     |       |      |      | 410   |       |       |        |      |
|    | cag  | gac   | ccc   | cag   | ctc   | ggc   | agg   | aca   | ctg | gcc   | agc  | ctg  | cag   | gct   | gag   | tac    | 1359 |
|    | Gln  | Asp   | Pro   | Gln   | Leu   | Gly   | Arg   | Thr   | Leu | Ala   | Ser  | Leu  | Gln   | Ala   | Glu   | Tyr    |      |
| 10 |      | 415   |       |       |       |       | 420   |       |     |       |      | 425  |       |       |       |        |      |
|    | cag  | gtg   | ctg   | gcc   | agc   | ctg   | gag   | ctg   | cag | gat   | ggt  | gag  | gac   | gag   | ggc   | tac    | 1407 |
|    | Gln  | Val   | Leu   | Ala   | Ser   | Leu   | Glu   | Leu   | Gln | Asp   | Gly  | Glu  | Asp   | Glu   | Gly   | Tyr    |      |
|    | 430  |       |       |       |       | 435   |       |       |     |       | 440  |      |       |       |       | 445    |      |
|    | ttc  | cag   | gag   | ctg   | ctg   | ggc   | tct   | gtc   | aac | agc   | ttg  | ctg  | aag   | gag   | ctg   | aga    | 1455 |
| L5 | Phe  | Gln   | Glu   | Leu   | Leu   | Gly   | Ser   | Val   | Asn | Ser   | Leu  | Leu  | Lys   | Glu   | Leu   | Arg    |      |
|    |      |       |       |       | 450   |       |       |       |     | 455   |      |      |       |       | 460   |        |      |
|    | tgaç | gcco  | cca c | cacca | aggad | et g  | gacto | gggat | gco | egcta | agtg | aggo | ctgag | ggg ( | gtgco | cagcgt | 1515 |
|    | gggt | gggd  | ett o | ctcag | gcag  | gg ag | gaca  | atctt | ggo | cagto | gctg | gctt | ggcc  | cat 1 | caaat | ggaaa  | 1575 |
|    | ccto | gaagg | jcc   |       |       |       |       |       |     |       |      |      |       |       |       |        | 1585 |
| 20 |      |       |       |       |       |       |       |       |     |       |      |      |       |       |       |        |      |
|    | <210 | )> 24 | l     |       |       |       |       |       |     |       |      |      |       |       |       |        |      |
|    | <211 | > 21  | .22   |       |       |       |       |       |     |       |      |      |       |       |       |        |      |
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|    | <b>\</b> 22 | 1> 0 | טט    |       |      |      |      |      |      |      |      |     |      |     |      |       |     |
|----|-------------|------|-------|-------|------|------|------|------|------|------|------|-----|------|-----|------|-------|-----|
|    | <22         | 2> ( | 56).  | . (19 | 99)  |      |      |      |      |      |      |     |      |     |      |       |     |
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|    | aga         | agca | ctg ( | ggcc  | ttgg | cc a | cago | aaca | c cc | actg | agca | cgc | tggg | agc | tgag | t atg | 58  |
| 5  |             |      |       |       |      |      |      |      |      |      |      |     |      |     |      | Met   |     |
|    |             |      |       |       |      |      |      |      |      |      |      |     |      |     |      | 1     |     |
|    | gcg         | tcc  | ctg   | gtc   | tcg  | ctg  | gag  | ctg  | ggg  | ctg  | ctt  | ctg | gct  | gtg | ctg  |       | 106 |
|    | Ala         | Ser  | Leu   | Val   | Ser  | Leu  | Glu  | Leu  | Gly  | Leu  | Leu  | Leu | Ala  | Val | Leu  | Val   |     |
|    |             |      |       | 5     |      |      |      |      | 10   |      |      |     |      | 15  |      |       |     |
| 10 | gtg         | acg  | gcg   | acg   | gcg  | tcc  | ccg  | cct  | gct  | ggt  | ctg  | ctg | agc  | ctg | ctc  | acc   | 154 |
|    | Val         | Thr  | Ala   | Thr   | Ala  | Ser  | Pro  | Pro  | Ala  | Gly  | Leu  | Leu | Ser  | Leu | Leu  | Thr   |     |
|    |             |      | 20    |       |      |      |      | 25   |      |      |      |     | 30   |     |      |       |     |
|    | tct         | ggc  | cag   | ggc   | gct  | ctg  | gat  | caa  | gag  | gct  | ctg  | ggc | ggc  | ctg | tta  | aat   | 202 |
|    | Ser         | Gly  | Gln   | Gly   | Ala  | Leu  | Asp  | Gln  | Glu  | Ala  | Leu  | Gly | Gly  | Leu | Leu  | Asn   |     |
| 15 |             | 35   |       |       |      |      | 40   |      |      | •    |      | 45  |      |     |      |       |     |
|    | acg         | ctg  | gcg   | gac   | cgt  | gtg  | cac  | tgc  | acc  | aac  | ggg  | ccg | tgt  | gga | aag  | tgc   | 250 |
|    | Thr         | Leu  | Ala   | Asp   | Arg  | Val  | His  | Cys  | Thr  | Asn  | Gly  | Pro | Cys  | Gly | Lys  | Cys   |     |
|    | 50          |      |       |       |      | 55   |      |      |      |      | 60   |     |      |     |      | 65    |     |
|    | ctg         | tct  | gtg   | gag   | gac  | gcc  | ctg  | ggc  | ctg  | ggc  | gag  | cct | gag  | ggg | tca  | ggg   | 298 |
| 20 | Leu         | Ser  | Val   | Glu   | Asp  | Ala  | Leu  | Gly  | Leu  | Gly  | Glu  | Pro | Glu  | Gly | Ser  | Gly   |     |
|    |             |      |       |       | 70   |      |      |      |      | 75   |      |     |      |     | 80   |       |     |
|    | ctg         | ccc  | ccg   | ggc   | ccg  | gtc  | ctg  | gag  | gcc  | agg  | tac  | gtc | gcc  | cgc | ctc  | agt   | 346 |
|    | Leu         | Pro  | Pro   | Gly   | Pro  | Val  | Leu  | Glu  | Ala  | Arg  | Tyr  | Val | Ala  | Arg | Leu  | Ser   |     |
|    |             |      |       | 85    |      |      |      |      | 90   |      |      |     |      | 95  |      |       |     |
| 25 | gcc         | gcc  | gcc   | gtc   | ctg  | tac  | ctc  | agc  | aac  | ccc  | gag  | ggc | acc  | tgt | gag  | gac   | 394 |

|    | Ala | Ala | Ala | Val | Leu | Tyr | Leu | Ser | Asn | Pro | Glu | Gly | Thr | Суѕ | Glu | Asp |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |     |     |
|    | act | cgg | gct | ggc | ctc | tgg | gcc | tct | cat | gca | gac | cac | ctc | ctg | gcc | ctg | 442 |
|    | Thr | Arg | Ala | Gly | Leu | Trp | Ala | Ser | His | Ala | Asp | His | Leu | Leu | Ala | Leu |     |
| 5  |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |     |     |
|    | ctc | gag | agc | ccc | aag | gcc | ctg | acc | ccg | ggc | ctg | agc | tgg | ctg | ctg | cag | 490 |
|    | Leu | Glu | Ser | Pro | Lys | Ala | Leu | Thr | Pro | Gly | Leu | Ser | Trp | Leu | Leu | Gln |     |
|    | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     | 145 |     |
|    | agg | atg | cag | gcc | cgg | gct | gcc | ggc | cag | acc | ccc | aag | acg | gcc | tgc | gta | 538 |
| 10 | Arg | Met | Gln | Ala | Arg | Ala | Ala | Gly | Gln | Thr | Pro | Lys | Thr | Ala | Cys | Val |     |
|    |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |     |     |
|    | gat | atc | cct | cag | ctg | ctg | gag | gag | gcg | gtg | ggg | gcg | ggg | gct | ccg | ggc | 586 |
|    | Asp | Ile | Pro | Gln | Leu | Leu | Glu | Glu | Ala | Val | Gly | Ala | Gly | Ala | Pro | Gly |     |
|    |     |     |     | 165 |     |     |     |     | 170 |     | •   |     |     | 175 |     |     |     |
| 15 | agt | gct | ggc | ggc | gtc | ctg | gct | gcc | ctg | ctg | gac | cat | gtc | agg | agc | ggg | 634 |
|    | Ser | Ala | Gly | Gly | Val | Leu | Ala | Ala | Leu | Leu | Asp | His | Val | Arg | Ser | Gly |     |
|    |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |     |     |
|    | tct | tgc | ttc | cac | gcc | ttg | ccg | agc | cct | cag | tac | ttc | gtg | gac | ttt | gtg | 682 |
|    | Ser | Cys | Phe | His | Ala | Leu | Pro | Ser | Pro | Gln | Tyr | Phe | Val | Asp | Phe | Val |     |
| 20 |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |     |     |
|    | ttc | cag | cag | cac | agc | agc | gag | gtc | cct | atg | acg | ctg | gcc | gag | ctg | tca | 730 |
|    | Phe | Gln | Gln | His | Ser | Ser | Glu | Val | Pro | Met | Thr | Leu | Ala | Glu | Leu | Ser |     |
|    | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     | 225 |     |
|    | gcc | ttg | atg | cag | cgc | ctg | ggg | gtg | ggc | agg | gag | gcc | cac | agt | gac | cac | 778 |
| 25 | Ala | Leu | Met | Gln | Arg | Leu | Gly | Val | Gly | Arg | Glu | Ala | His | Ser | Asp | His |     |

|    |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |       |      |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------|------|
|    | agt | cat | cgg | cac | agg | gga | gcc | agc | agc | cgg | gac | cct | gtg | ccc | ctc | atc   | 826  |
|    | Ser | His | Arg | His | Arg | Gly | Ala | Ser | Ser | Arg | Asp | Pro | Val | Pro | Leu | Ile   |      |
|    |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |       |      |
| 5  | agc | tcc | agc | aac | agc | tcc | agt | gtg | tgg | gac | acg | gta | tgc | ctg | agt | gcc   | 874  |
|    | Ser | Ser | Ser | Asn | Ser | Ser | Ser | Val | Trp | Asp | Thr | Val | Cys | Leu | Ser | Ala   |      |
|    |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |       |      |
|    | agg | gac | gtg | atg | gct | gca | tat | gga | ctg | tcg | gaa | cag | gct | ggg | gtg | acc   | 922  |
|    | Arg | Asp | Val | Met | Ala | Ala | Tyr | Gly | Leu | Ser | Glu | Gln | Ala | Gly | Val | Thr   |      |
| 10 |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |       |      |
|    | ccg | gag | gcc | tgg | gcc | caa | ctg | agc | cct | gcc | ctg | ctc | caa | cag | cag | ctg   | 970  |
|    | Pro | Glu | Ala | Trp | Ala | Gln | Leu | Ser | Pro | Ala | Leu | Leu | Gln | Gln | Gln | Leu   |      |
|    | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     | 305   |      |
|    | agt | gga | gcc | tgc | acc | tcc | cag | tcč | agg | ccc | ccc | gtc | cag | gac | cag | ctc · | 1018 |
| 15 | Ser | Gly | Ala | Cys | Thr | Ser | Gln | Ser | Arg | Pro | Pro | Val | Gln | Asp | Gln | Leu   |      |
|    |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |       |      |
|    | agc | cag | tca | gag | agg | tat | ctg | tac | ggc | tcc | ctg | gcc | acg | ctg | ctc | atc   | 1066 |
|    | Ser | Gln | Ser | Glu | Arg | Tyr | Leu | Tyr | Gly | Ser | Leu | Ala | Thr | Leu | Leu | Ile   |      |
|    |     |     |     | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |       |      |
| 20 | tgc | ctc | tgc | gcg | gtc | ttt | ggc | ctc | ctg | ctg | ctg | acc | tgc | act | ggc | tgc   | 1114 |
|    | Cys | Leu | Cys | Ala | Val | Phe | Gly | Leu | Leu | Leu | Leu | Thr | Cys | Thr | Gly | Cys   |      |
|    |     |     | 340 |     |     |     |     | 345 |     |     |     |     | 350 |     |     |       |      |
|    | agg | ggg | gtc | gcc | cac | tac | atc | ctg | cag | acc | ttc | ctg | agc | ctg | gca | gtg   | 1162 |
|    | Arg | Gly | Val | Ala | His | Tyr | Ile | Leu | Gln | Thr | Phe | Leu | Ser | Leu | Ala | Val   |      |
| 25 |     | 355 |     |     |     |     | 360 |     |     |     |     | 365 |     |     |     |       |      |

|    | ggt | gca | ctc | act | ggg | gac | gct | gtc | ctg | cat | ctg | acg | ccc | aag | gtg | ctg | 1210 |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|    | Gly | Ala | Leu | Thr | Gly | Asp | Ala | Val | Leu | His | Leu | Thr | Pro | Lys | Val | Leu |      |
|    | 370 |     |     |     |     | 375 |     |     |     |     | 380 |     |     |     |     | 385 |      |
|    | ggg | ctg | cat | aca | cac | agc | gaa | gag | ggc | ctc | agc | cca | cag | ccc | acc | tgg | 1258 |
| 5  | Gly | Leu | His | Thr | His | Ser | Glu | Glu | Gly | Leu | Ser | Pro | Gln | Pro | Thr | Trp |      |
|    |     |     |     |     | 390 |     |     |     |     | 395 |     |     |     |     | 400 |     |      |
|    | cgc | ctc | ctg | gct | atg | ctg | gcc | ggg | ctc | tac | gcc | ttc | ttc | ctg | ttt | gag | 1306 |
|    | Arg | Leu | Leu | Ala | Met | Leu | Ala | Gly | Leu | Tyr | Ala | Phe | Phe | Leu | Phe | Glu |      |
|    |     |     |     | 405 |     |     |     |     | 410 |     |     |     |     | 415 |     |     |      |
| 10 | aac | ctc | ttc | aat | ctc | ctg | ctg | ccc | agg | gac | ccg | gag | gac | ctg | gag | gac | 1354 |
|    | Asn | Leu | Phe | Asn | Leu | Leu | Leu | Pro | Arg | Asp | Pro | Glu | Asp | Leu | Glu | Asp |      |
|    |     |     | 420 |     |     |     |     | 425 |     |     |     |     | 430 |     |     |     |      |
|    | ggg | ccc | tgc | ggc | cac | agc | agc | cat | agc | cac | ggg | ggc | cac | agc | cac | ggt | 1402 |
|    | Gly | Pro | Cys | Gly | His | Ser | Ser | His | Ser | His | Gly | Gly | His | Ser | His | Gly |      |
| 15 |     | 435 |     |     |     |     | 440 |     |     |     |     | 445 |     |     |     |     |      |
|    | gtg | tcc | ctg | cag | ctg | gca | ccc | agc | gag | ctc | cgg | cag | ccc | aag | ccc | ccc | 1450 |
|    | Val | Ser | Leu | Gln | Leu | Ala | Pro | Ser | Glu | Leu | Arg | Gln | Pro | Lys | Pro | Pro |      |
|    | 450 |     |     |     |     | 455 |     |     |     |     | 460 |     |     |     |     | 465 |      |
|    | cac | gag | ggc | tcc | cgc | gca | gac | ctg | gtg | gcg | gag | gag | agc | ccg | gag | ctg | 1498 |
| 20 | His | Glu | Gly | Ser | Arg | Ala | Asp | Leu | Val | Ala | Glu | Glu | Ser | Pro | Glu | Leu |      |
|    |     |     |     |     | 470 |     |     |     |     | 475 |     |     |     |     | 480 |     |      |
|    | ctg | aac | cct | gag | ccc | agg | aga | ctg | agc | cca | gag | ttg | agg | cta | ctg | ccc | 1546 |
|    | Leu | Asn | Pro | Glu | Pro | Arg | Arg | Leu | Ser | Pro | Glu | Leu | Arg | Leu | Leu | Pro |      |
|    |     |     |     | 485 |     |     |     |     | 490 |     |     |     |     | 495 |     |     |      |
| 25 | tat | atg | atc | act | ctg | ggc | gac | gcc | gtg | cac | aac | ttc | gcc | gac | ggg | ctg | 1594 |

0

|    | Tyr | Met | Ile | Thr | Leu | Gly | Asp | Ala | Val | His | Asn | Phe | Ala | Asp | Gly | Leu |      |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|    |     |     | 500 |     |     |     |     | 505 |     |     |     |     | 510 |     |     |     |      |
|    | gcc | gtg | ggc | gcc | gcc | ttc | gcg | tcc | tcc | tgg | aag | acc | ggg | ctg | gcc | acc | 1642 |
|    | Ala | Val | Gly | Ala | Ala | Phe | Ala | Ser | Ser | Trp | Lys | Thr | Gly | Leu | Ala | Thr |      |
| 5  |     | 515 |     |     |     |     | 520 |     |     |     |     | 525 |     |     |     |     | ٠    |
|    | tcg | ctg | gcc | gtg | ttc | tgc | cac | gag | ttg | cca | cac | gag | ctg | ggg | gac | ttc | 1690 |
|    | Ser | Leu | Ala | Val | Phe | Cys | His | Glu | Leu | Pro | His | Glu | Leu | Gly | Asp | Phe |      |
|    | 530 |     |     |     |     | 535 |     |     |     |     | 540 |     |     |     |     | 545 |      |
|    | gcc | gcc | ttg | ctg | cac | gcg | ggg | ctg | tcc | gtg | cgc | caa | gca | ctg | ctg | ctg | 1738 |
| 10 | Ala | Ala | Leu | Leu | His | Ala | Gly | Leu | Ser | Val | Arg | Gln | Ala | Leu | Leu | Leu |      |
|    |     |     |     |     | 550 |     |     |     |     | 555 |     |     |     |     | 560 |     |      |
|    | aac | ctg | gcc | tcc | gcg | ctc | acg | gcc | ttc | gct | ggt | ctc | tac | gtg | gca | ctc | 1786 |
|    | Asn | Leu | Ala | Ser | Ala | Leu | Thr | Ala | Phe | Ala | Gly | Leu | Tyr | Val | Ala | Leu |      |
|    |     |     |     | 565 |     |     | •   |     | 570 |     |     |     |     | 575 |     |     |      |
| 15 | gcg | gtt | gga | gtc | agc | gag | gag | agc | gag | gcc | tgg | atc | ctg | gca | gtg | gcc | 1834 |
|    | Ala | Val | Gly | Val | Ser | Glu | Glu | Ser | Glu | Ala | Trp | Ile | Leu | Ala | Val | Ala |      |
|    |     |     | 580 |     |     |     |     | 585 |     |     |     |     | 590 |     |     |     |      |
|    | acc | ggc | ctg | ttc | ctc | tac | gta | gca | ctc | tgc | gac | atg | ctc | ccg | gcg | atg | 1882 |
|    | Thr | Gly | Leu | Phe | Leu | Tyr | Val | Ala | Leu | Cys | Asp | Met | Leu | Pro | Ala | Met |      |
| 20 |     | 595 |     |     |     |     | 600 |     |     |     |     | 605 |     |     |     |     |      |
|    | ttg | aaa | gta | cgg | gac | ccg | cgg | ccc | tgg | ctc | ctc | ttc | ctg | ctg | cac | aac | 1930 |
|    | Leu | Lys | Val | Arg | Asp | Pro | Arg | Pro | Trp | Leu | Leu | Phe | Leu | Leu | His | Asn |      |
|    | 610 |     |     |     |     | 615 |     |     |     |     | 620 |     |     |     |     | 625 |      |
|    | gtg | ggc | ctg | ctg | ggc | ggc | tgg | acc | gtc | ctg | ctg | ctg | ctg | tcc | ctg | tac | 1978 |
| 25 | Val | Gly | Leu | Leu | Gly | Gly | Trp | Thr | Val | Leu | Leu | Leu | Leu | Ser | Leu | Tvr |      |

54 /346

630 635 640 gag gat gac atc acc ttc tgataccctg ccctagtccc ccacctttga 2026 Glu Asp Asp Ile Thr Phe 645 5 cttaagatcc cacacctcac aaacctacag cccagaaacc agaagcccct atagaggecc 2086 cagteccaac tecagtaaag acactettgt cettgg 2122 <210> 25 <211> 1775 10 <212> DNA <213> Homo sapiens <220> <221> CDS <222> (62)..(1402) 15 <400> 25 aaaacaagcc gggtggctga gccaggctgt gcacggagtg cctgacgggc ccaacagacc 60 c atg ctg cat cca gag acc tcc cct ggc cgg ggg cat ctc ctg gct gtg 109 Met Leu His Pro Glu Thr Ser Pro Gly Arg Gly His Leu Leu Ala Val 1 5 10 15

ctg cag gag cag gct ccg atg gcc gga gcc ctg aac agg aag gag agt 205
Leu Gln Glu Gln Ala Pro Met Ala Gly Ala Leu Asn Arg Lys Glu Ser

ctc ctg gcc ctc ctt ggc acc gcc tgg gca gag gtg tgg cca ccc cag

Leu Leu Ala Leu Leu Gly Thr Ala Trp Ala Glu Val Trp Pro Pro Gln

157

25 35 40 45

20

|    | ttc | ttg | ctc | ctc | tcc | ctg | cac | aac | cgc | ctg | cgc | agc  | tgg | gtc | cag | ccc | 253 |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|
|    | Phe | Leu | Leu | Leu | Ser | Leu | His | Asn | Arg | Leu | Arg | Ser  | Trp | Val | Gln | Pro |     |
|    |     | 50  |     |     |     |     | 55  |     |     |     |     | 60   |     |     |     |     |     |
|    | cct | gcg | gct | gac | atg | cgg | agg | ctg | gac | tgg | agt | gac  | agc | ctg | gcc | caa | 301 |
| 5  | Pro | Ala | Ala | Asp | Met | Arg | Arg | Leu | Asp | Trp | Ser | Asp  | Ser | Leu | Ala | Gln |     |
|    | 65  |     |     |     |     | 70  |     |     |     |     | 75  |      |     |     |     | 80  |     |
|    | ctg | gct | caa | gcc | agg | gca | gcc | ctc | tgt | gga | atc | cca  | acc | ccg | agc | ctg | 349 |
|    | Leu | Ala | Gln | Ala | Arg | Ala | Ala | Leu | Cys | Gly | Ile | Pro  | Thr | Pro | Ser | Leu |     |
|    |     |     |     |     | 85  |     |     |     |     | 90  |     |      |     |     | 95  | •   |     |
| 10 | gcg | tcc | ggc | ctg | tgg | cgc | acc | ctg | caa | gtg | ggc | tgg  | aac | atg | cag | ctg | 397 |
|    | Ala | Ser | Gly | Leu | Trp | Arg | Thr | Leu | Gln | Val | Gly | Trp  | Asn | Met | Gln | Leu |     |
|    |     |     |     | 100 |     |     |     |     | 105 |     |     |      |     | 110 |     |     |     |
|    | ctg | ccc | gcg | ggc | ttg | gcg | tcc | ttt | gtt | gaa | gtg | gtc  | agc | cta | tgg | ttt | 445 |
|    | Leu | Pro | Ala | Gly | Leu | Ala | Ser | Phe | Val | Glu | Val | Val  | Ser | Leu | Trp | Phe |     |
| 15 |     |     | 115 |     |     |     |     | 120 |     |     |     |      | 125 |     |     |     |     |
|    | gca | gag | ggg | cag | cgg | tac | agc | cac | gcg | gca | gga | gag  | tgt | gct | cgc | aac | 493 |
|    | Ala | Glu | Gly | Gln | Arg | Tyr | Ser | His | Ala | Ala | Gly | Glu  | Cys | Ala | Arg | Asn |     |
|    |     | 130 |     |     |     |     | 135 |     |     |     |     | 140  |     |     |     |     |     |
|    | gcc | acc | tgc | acc | cac | tac | acg | cag | ctc | gtg | tgg | gcc  | acc | tca | agc | cag | 541 |
| 20 | Ala | Thr | Cys | Thr | His | Tyr | Thr | Gln | Leu | Val | Trp | Ala  | Thr | Ser | Ser | Gln |     |
| •  | 145 |     |     |     |     | 150 |     |     |     |     | 155 |      |     |     |     | 160 |     |
|    | ctg | ggc | tgt | ggg | cgg | cac | ctg | tgc | tct | gca | ggc | cag  | gca | gcg | ata | gaa | 589 |
|    | Leu | Gly | Cys | Gly | Arg | His | Leu | Cys | Ser | Ala | Gly | Gln  | Ala | Ala | Ile | Glu |     |
|    |     |     |     |     | 165 |     |     |     |     | 170 |     |      |     |     | 175 |     |     |
| 25 | gcc | ttt | qtc | tat | acc | tac | tcc | ccc | ασa | aac | aac | t.aa | πασ | atc | aac | aaa | 637 |

|    | Ala | Phe | Val | Cys | Ala | Tyr | Ser | Pro | Gly | Gly | Asn | Trp | Glu | Val | Asn | Gly   |      |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------|------|
|    |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |       |      |
|    | aag | aca | atc | atc | ccc | tat | aag | aag | ggt | gcc | tgg | tgt | tcg | ctc | tgc | aca , | 685  |
|    | Lys | Thr | Ile | Ile | Pro | Tyr | Lys | Lys | Gly | Ala | Trp | Cys | Ser | Leu | Cys | Thr   |      |
| 5  |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |       |      |
|    | gcc | agt | gtc | tca | ggc | tgc | ttc | aaa | gcc | tgg | gac | cat | gca | ggg | ggg | ctc   | 733  |
|    | Ala | Ser | Val | Ser | Gly | Cys | Phe | Lys | Ala | Trp | Asp | His | Ala | Gly | Gly | Leu   |      |
|    |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |       |      |
|    | tgt | gag | gtc | ccc | agg | aat | cct | tgt | cgc | atg | agc | tgc | cag | aac | cat | gga   | 781  |
| 10 | Cys | Glu | Val | Pro | Arg | Asn | Pro | Cys | Arg | Met | Ser | Cys | Gln | Asn | His | Gly   |      |
|    | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240   |      |
|    | cgt | ctc | aac | atc | agc | acc | tgc | cac | tgc | cac | tgt | ccc | cct | ggc | tac | acg   | 829  |
|    | Arg | Leu | Asn | Ile | Ser | Thr | Cys | His | Cys | His | Cys | Pro | Pro | Gly | Tyr | Thr   |      |
|    |     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |       |      |
| 15 | ggc | aga | tac | tgc | caa | gtg | agg | tgc | agc | ctg | cag | tgt | gtg | cac | ggc | cgg   | 877  |
|    | Gly | Arg | Tyr | Cys | Gln | Val | Arg | Cys | Ser | Leu | Gln | Cys | Val | His | Gly | Arg   |      |
|    |     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |       |      |
|    | ttc | cgg | gag | gag | gag | tgc | tcg | tgc | gtc | tgt | gac | atc | ggc | tac | ggg | gga   | 925  |
|    | Phe | Arg | Glu | Glu | Glu | Cys | Ser | Cys | Val | Cys | Asp | Ile | Gly | Tyr | Gly | Gly   |      |
| 20 |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |       |      |
|    | gcc | cag | tgt | gcc | acc | aag | gtg | cat | ttt | ccc | ttc | cac | acc | tgt | gac | ctg   | 973  |
|    | Ala | Gln | Cys | Ala | Thr | Lys | Val | His | Phe | Pro | Phe | His | Thr | Cys | Asp | Leu   |      |
| •  |     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |       |      |
|    | agg | atc | gac | gga | gac | tgc | ttc | atg | gtg | tct | tca | gag | gca | gac | acc | tat   | 1021 |
| 25 | Arg | Ile | Asp | Gly | Asp | Суз | Phe | Met | Val | Ser | Ser | Glu | Ala | Asp | Thr | Tyr   |      |

|    | 305 |     |     |     |     | 310 |     |     |     |     | 315 |                 |     |     |     | 320 |      |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----------------|-----|-----|-----|-----|------|
|    | tac | aga | gcc | agg | atg | aaa | tgt | cag | agg | aaa | ggc | ggg             | gtg | ctg | gcc | cag | 1069 |
|    | Tyr | Arg | Ala | Arg | Met | Lys | Cys | Gln | Arg | Lys | Gly | Gly             | Val | Leu | Ala | Gln |      |
|    |     |     |     |     | 325 |     |     |     |     | 330 |     |                 |     |     | 335 |     |      |
| 5  | atc | aag | agc | cag | aaa | gtg | cag | gac | atc | ctc | gcc | ttc             | tat | ctg | ggc | cgc | 1117 |
|    | Ile | Lys | Ser | Gln | Lys | Val | Gln | Asp | Ile | Leu | Ala | Phe             | Tyr | Leu | Gly | Arg |      |
|    |     |     |     | 340 |     |     |     |     | 345 |     |     |                 |     | 350 |     |     |      |
|    | ctg | gag | acc | acc | aac | gag | gtg | att | gac | agt | gac | ttc             | gag | acc | agg | aac | 1165 |
|    | Leu | Glu | Thr | Thr | Asn | Glu | Val | Ile | Asp | Ser | Asp | Phe             | Glu | Thr | Arg | Asn |      |
| 10 |     |     | 355 |     |     |     |     | 360 |     |     |     | ٠               | 365 |     |     |     |      |
|    | ttc | tgg | atc | ggg | ctc | acc | tac | aag | acc | gcc | aag | gac             | tcc | ttc | cgc | tgg | 1213 |
|    | Phe | Trp | Ile | Gly | Leu | Thr | Tyr | Lys | Thr | Ala | Lys | Asp             | Ser | Phe | Arg | Trp |      |
|    |     | 370 |     |     |     |     | 375 |     |     |     |     | 380 <sub></sub> |     |     |     |     |      |
|    | gcc | aca | ggg | gag | cac | cag | gcc | ttc | acc | agt | ttt | gcc             | ttt | ggg | cag | cct | 1261 |
| 15 | Ala | Thr | Gly | Glu | His | Gln | Ala | Phe | Thr | Ser | Phe | Ala             | Phe | Gly | Gln | Pro |      |
|    | 385 |     |     |     |     | 390 |     |     |     |     | 395 |                 |     | •   |     | 400 |      |
|    | gac | aac | cac | ggg | ttt | ggc | aac | tgc | gtg | gag | ctg | cag             | gct | tca | gct | gcc | 1309 |
|    | Asp | Asn | His | Gly | Phe | Gly | Asn | Cys | Val | Glu | Leu | Gln             | Ala | Ser | Ala | Ala |      |
|    |     |     |     |     | 405 |     | •   |     |     | 410 |     |                 |     |     | 415 |     |      |
| 20 | ttc | aac | tgg | aac | aac | cag | cgc | tgc | aaa | acc | cga | aac             | cgt | tac | atc | tgc | 1357 |
|    | Phe | Asn | Trp | Asn | Asn | Gln | Arg | Cys | Lys | Thr | Arg | Asn             | Arg | Tyr | Ile | Cys |      |
|    |     |     |     | 420 |     |     |     |     | 425 |     |     |                 |     | 430 |     |     |      |
|    | cag | ttt | gcc | cag | gag | cac | atc | tcc | cgg | tgg | ggc | cca             | ggg | tcc |     |     | 1399 |
|    | Gln | Phe | Ala | Gln | Glu | His | Ile | Ser | Arg | Trp | Gly | Pro             | Gly | Ser |     |     |      |
| 25 |     |     | 435 |     |     |     |     | 440 |     |     |     |                 | 445 |     |     |     |      |

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tgaggcetga ccacatgget ccctcgcctg ccctgggage accggctctg cttacctgte 1459
cgcccacctg tctggaacaa gggccaggtt aagaccacat gcctcatgtc caaagaggtc 1519
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tcaattagat ggcaaaggag aggacaccge cagtggtcca aaaaggctge tctctccac 1699
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tegetggtgg gtggacteet gggegetgeg eggageegeg eeggetgggt tagegeggge 180
ggggegetta gteceaceec cagaggagge ggaagaggag eeegageetg geegeggget 240
gggeeeegee geageteeag etggeegget tggteetgeg gteeettete tgggaggeec 300
gaceeeggee gegeeeagee eeeace atg eea eee geg ggg ete ege egg gee 353
Met Pro Pro Ala Gly Leu Arg Arg Ala

1 5

gcg ccg ctc acc gca atc gct ctg ttg gtg ctg ggg gct ccc ctg gtg 401

|    | Ala | Pro | Leu | Thr | Ala | Ile | Ala | Leu | Leu | Val | Leu | Gly | Ala | Pro | Leu | Val |                  |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------------------|
|    | 10  |     |     |     |     | 15  |     |     |     |     | 20  |     |     |     |     | 25  |                  |
|    | ctg | gcc | ggc | gag | gac | tgc | ctg | tgg | tac | ctg | gac | cgg | aat | ggc | tcc | tgg | 449              |
|    | Leu | Ala | Gly | Glu | Asp | Cys | Leu | Trp | Tyr | Leu | Asp | Arg | Asn | Gly | Ser | Trp |                  |
| 5  |     |     |     |     | 30  |     |     |     |     | 35  |     |     |     |     | 40  |     |                  |
|    | cat | ccg | ggg | ttt | aac | tgc | gag | ttc | ttc | acc | ttc | tgc | tgc | ggg | acc | tgc | 497              |
|    | His | Pro | Gly | Phe | Asn | Суѕ | Glu | Phe | Phe | Thr | Phe | Cys | Cys | Gly | Thr | Cys |                  |
|    |     |     |     | 45  |     |     |     |     | 50  |     |     |     |     | 55  |     |     |                  |
|    | tac | cat | cgg | tac | tgc | tgc | agg | gac | ctg | acc | ttg | ctt | atc | acc | gag | agg | 545              |
| 10 | Tyr | His | Arg | Tyr | Cys | Суѕ | Arg | Asp | Leu | Thr | Leu | Leu | Ile | Thr | Glu | Arg |                  |
|    |     |     | 60  |     |     |     |     | 65  |     |     |     |     | 70  |     |     |     |                  |
|    | cag | cag | aag | cac | tgc | ctg | gcc | ttc | agc | ccc | aag | acc | ata | gca | ggc | atc | 593 <sup>°</sup> |
|    | Gln | Gln | Lys | His | Cys | Leu | Ala | Phe | Ser | Pro | Lys | Thr | Ile | Ala | Gly | Ile |                  |
|    |     | 75  |     |     |     |     | 80  |     |     |     |     | 85  |     |     |     |     |                  |
| 15 |     |     |     | gtg |     |     |     |     |     |     |     |     |     |     |     |     | 641              |
|    |     | Ser | Ala | Val | Ile | Leu | Phe | Val | Ala | Val | Val | Ala | Thr | Thr | Ile | Суѕ |                  |
|    | 90  |     |     |     |     | 95  |     |     |     |     | 100 |     |     |     |     | 105 |                  |
|    |     | •   |     | tgt |     |     |     |     |     |     |     |     |     |     |     |     | 689              |
|    | Cys | Phe | Leu | Cys |     | Cys | Cys | Tyr | Leu | Tyr | Arg | Arg | Arg | Gln | Gln | Leu |                  |
| 20 |     |     |     |     | 110 |     |     |     |     | 115 |     |     |     |     | 120 |     |                  |
|    |     |     |     | ttt |     |     |     |     |     |     |     |     |     |     |     |     | 737              |
|    | Gln | Ser | Pro | Phe | Glu | Gly | Gln | Glu |     | Pro | Met | Thr | Gly | Ile | Pro | Val |                  |
|    |     |     |     | 125 |     |     |     |     | 130 |     |     |     |     | 135 |     |     |                  |
| 25 |     |     |     | tac |     |     |     |     |     |     |     |     |     |     |     |     | 785              |
| 25 | Gin | Pro | val | Tyr | Pro | Tyr | Pro | Gln | asA | Pro | Lvs | Ala | Glv | Pro | Ala | Pro |                  |

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|                | 14          | 0         |           | 1.45      |          | 150         |            |      |
|----------------|-------------|-----------|-----------|-----------|----------|-------------|------------|------|
|                | 14.         | U         |           | 145       |          | 150         |            |      |
|                | cca cag cc  | t ggc ttc | ata tac   | cca cct   | agt ggt  | cct gct ccc | caa tat    | 833  |
|                | Pro Gln Pro | o Gly Phe | Ile Tyr   | Pro Pro   | Ser Gly  | Pro Ala Pro | Gln Tyr    |      |
|                | 155         |           | 160       |           |          | 165         |            |      |
| 5 <sub>.</sub> | cca ctc ta  | c cca gct | ggg ccc   | cca gtc   | tac aac  | cct gca gct | cct cct    | 881  |
|                | Pro Leu Ty  | r Pro Ala | Gly Pro   | Pro Val   | Tyr Asn  | Pro Ala Ala | Pro Pro    |      |
|                | 170         |           | 175       |           | 180      |             | 185        |      |
|                | ccc tat at  | g cca cca | cag ccc   | tct tac   | ccg gga  | gcc tgaggaa | .cca       | 927  |
|                | Pro Tyr Me  | t Pro Pro | Gln Pro   | Ser Tyr   | Pro Gly  | Ala         |            |      |
| 10             |             | 190       |           |           | 195      |             |            |      |
|                | gccatgtctc  | tgctgccc  | ct tcagto | gatge caa | accttggg | agatgccctc  | atcctgtacc | 987  |
|                | tgcatctggt  | cctggggg  | tg gcagga | agtcc tc  | cagecace | aggccccaga  | ccaagccaag | 1047 |
|                | ccctgggccc  | tactgggg  | ac agagco | cccag gga | agtggaa  | caggagetga  | actagaacta | 1107 |
|                | tgaggggttg  | gggggagg  | gc ttggaa | attat ggg | gctatttt | tactgggggc  | aagggaggga | 1167 |
| 15             | gatgacagcc  | tgggtcaca | ag tgcctg | gtttt caa | atagtcc  | ctctgctccc  | aagatcccag | 1227 |
|                | ccaggaaggc  | tggggccct | a ctgttt  | tgtcc cct | ctgggct  | ggggtggggg  | gagggaggag | 1287 |
|                | gttccgtcag  | cagetgge  | ag tagcco | ctcct ctc | tggctgc  | cccactggcc  | acatctctgg | 1347 |
|                | cctgctagat  | taaagctgl | a aagac   |           |          |             |            | 1372 |
|                |             |           |           |           |          |             |            |      |
| 20             | <210> 27    |           |           |           |          |             |            |      |
|                | <211> 2074  |           |           |           |          |             |            |      |
|                | <212> DNA   | •         |           |           |          |             |            |      |
|                | <213> Homo  | sapiens   |           |           |          |             |            |      |
|                | <220>       |           |           |           |          |             |            |      |

25

<221> CDS

|    | <22 | 2> ( | 101)  | (1   | 723)  |      |                   |      |       |      |      |     |      |       |      |        |     |
|----|-----|------|-------|------|-------|------|-------------------|------|-------|------|------|-----|------|-------|------|--------|-----|
|    | <40 | 0> 2 | 7     |      |       |      |                   |      |       |      |      |     |      |       |      |        |     |
|    | ctt | tagg | gtg ( | cgcg | ggtg  | ca g | tata <sup>.</sup> | tctc | g cg  | ctct | ctcc | cct | ttcc | ccc i | tccc | ctttcc | 60  |
|    | cca | cccc | ggg ( | eget | caggi | tt g | gtct              | ggac | c gga | aagc | gaag | atg | gcg  | act   | tct  | ggc    | 115 |
| 5  |     |      |       |      |       |      |                   |      |       |      |      | Met | Ala  | Thr   | Ser  | Gly    |     |
|    |     |      |       |      |       |      |                   |      |       |      |      | 1   |      |       |      | 5      |     |
|    | gcg | gcc  | tcg   | gcg  | gag   | ctg  | gtg               | atc  | ggc   | tgg  | tgc  | ata | ttc  | ggc   | ctc  | tta    | 163 |
|    | Ala | Ala  | Ser   | Ala  | Glu   | Leu  | Val               | Ile  | Gly   | Trp  | Cys  | Ile | Phe  | Gly   | Leu  | Leu    |     |
|    |     |      | -     |      | 10    |      |                   |      |       | 15   |      |     |      |       | 20   |        |     |
| 10 | cta | ctg  | gct   | att  | ttg   | gca  | ttc               | tgc  | tgg   | ata  | tat  | gtt | cgt  | aaa   | tac  | caa    | 211 |
|    | Leu | Leu  | Ala   | Ile  | Leu   | Ala  | Phe               | Cys  | Trp   | Ile  | Tyr  | Val | Arg  | Lys   | Tyr  | Gln    |     |
|    |     |      |       | 25   |       |      |                   |      | 30    |      |      |     |      | 35    |      |        |     |
|    | agt | cgg  | cgg   | gaa  | agt   | gaa  | gtt               | gtc  | tcc   | acc  | ata  | aca | gca  | att   | ttt  | tct    | 259 |
|    | Ser | Arg  | Arg   | Glu  | Ser   | Glu  | Val               | Val  | Ser   | Thr  | Ile  | Thr | Ala  | Ile   | Phe  | Ser    |     |
| 15 |     |      | 40    | •    |       |      |                   | 45   |       |      |      |     | 50   |       |      |        |     |
|    | cta | gca  | att   | gca  | ctt   | atc  | aca               | tca  | gca   | ctt  | cta  | cca | gtg  | gat   | ata  | ttt    | 307 |
|    | Leu | Ala  | Ile   | Ala  | Leu   | Ile  | Thr               | Ser  | Ala   | Leu  | Leu  | Pro | Val  | Asp   | Ile  | Phe    |     |
|    |     | 55   |       |      |       |      | 60                |      |       |      |      | 65  |      |       |      |        |     |
|    | ttg | gtt  | tct   | tac  | atg   | aaa  | aat               | caa  | aat   | ggt  | aca  | ttt | aag  | gac   | tgg  | gct    | 355 |
| 20 | Leu | Val  | Ser   | Tyr  | Met   | Lys  | Asn               | Gln  | Asn   | Gly  | Thr  | Phe | Lys  | Asp   | Trp  | Ala    |     |
|    | 70  |      |       |      |       | 75   |                   |      |       |      | 80   |     |      |       |      | 85     |     |
|    | aat | gct  | aat   | gtc  | agc   | aga  | cag               | att  | gag   | gac  | act  | gta | tta  | tac   | ggt  | tac    | 403 |
|    | Asn | Ala  | Asn   | Val  | Ser   | Arg  | Gln               | Ile  | Glu   | Asp  | Thr  | Val | Leu  | Tyr   | Gly  | Tyr    |     |
|    |     |      |       |      | 90    |      |                   |      |       | 95   |      |     |      |       | 100  |        |     |
| 25 | tat | act  | tta   | tat  | tct   | gtt  | ata               | ttg  | ttc   | tgt  | gtg  | ttc | ttc  | tgg   | atc  | cct    | 451 |

|    | Tyr | Thr | Leu | Tyr | Ser | Val | Ile | Leu | Phe | Cys | Val | Phe | Phe | Trp | Ile | Pro |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    |     |     |     | 105 |     |     |     |     | 110 |     |     |     |     | 115 |     |     |     |
|    | ttt | gtc | tac | ttc | tat | tat | gaa | gaa | aag | gat | gat | gat | gat | act | agt | aaa | 499 |
|    | Phe | Val | Tyr | Phe | Tyr | Tyr | Glu | Glu | Lys | Asp | Asp | Asp | Asp | Thr | Ser | Lys |     |
| 5  |     |     | 120 |     |     |     |     | 125 |     |     |     |     | 130 |     |     |     |     |
|    | tgt | act | caa | att | aaa | acg | gca | ctc | aag | tat | act | ttg | gga | ttt | gtt | gtg | 547 |
|    | Cys | Thr | Gln | Ile | Lys | Thr | Ala | Leu | Lys | Tyr | Thr | Leu | Gly | Phe | Val | Val |     |
|    |     | 135 |     |     |     |     | 140 |     |     |     |     | 145 |     |     |     |     |     |
|    | att | tgt | gca | ctg | ctt | ctt | tta | gtt | ggt | gcc | ttt | gtt | cca | ťtg | aat | gtt | 595 |
| 10 | Ile | Суз | Ala | Leu | Leu | Leu | Leu | Val | Gly | Ala | Phe | Val | Pro | Leu | Asn | Val |     |
|    | 150 | •   |     |     |     | 155 |     |     |     |     | 160 |     |     |     | •   | 165 |     |
|    | CCC | aat | aac | aaa | aat | tct | aca | gag | tgg | gaa | aaa | gtg | aag | tcc | cta | ttt | 643 |
|    | Pro | Asn | Asn | Lys | Asn | Ser | Thr | Glu | Trp | Glu | Lys | Val | Lys | Ser | Leu | Phe |     |
|    |     |     |     |     | 170 |     |     |     |     | 175 |     |     |     |     | 180 |     |     |
| 15 | gaa | gaa | ctt | gga | agt | agt | cat | ggt | tta | gct | gca | ttg | tca | ttt | tct | atc | 691 |
|    | Glu | Glu | Leu | Gly | Ser | Ser | His | Gly | Leu | Ala | Ala | Leu | Ser | Phe | Ser | Ile |     |
|    |     |     |     | 185 |     |     |     |     | 190 |     |     |     |     | 195 |     |     |     |
|    | agt | tct | ctg | acc | ttg | att | gga | atg | ttg | gca | gct | ata | act | tac | aca | gcc | 739 |
|    | Ser | Ser | Leu | Thr | Leu | Ile | Gly | Met | Leu | Ala | Ala | Ile | Thr | Tyr | Thr | Ala |     |
| 20 |     |     | 200 |     |     |     |     | 205 |     |     |     |     | 210 |     |     |     |     |
|    | tat | ggc | atg | tct | gcg | tta | cct | tta | aat | ctg | ata | aaa | ggc | act | aga | agc | 787 |
|    | Tyr | Gly | Met | Ser | Ala | Leu | Pro | Leu | Asn | Leu | Ile | Lys | Gly | Thr | Arg | Ser |     |
|    |     | 215 |     |     |     |     | 220 |     |     |     |     | 225 |     |     |     |     |     |
|    | gct | gct | tat | gaa | cgt | ttg | gaa | aac | act | gaa | gac | att | gaa | gaa | gta | gaa | 835 |
| 25 | Ala | Ala | Tyr | Glu | Arg | Leu | Glu | Asn | Thr | Glu | Asp | Ile | Glu | Glu | Val | Glu |     |

|    | 230 |     |     |     |     | 235 |     |     |     |     | 240 |     |     |     |     | 245 |      |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|    | caa | cac | att | caa | acg | att | aaa | tca | aaa | agc | aaa | gat | ggt | cga | cct | ttg | 883  |
|    | Gln | His | Ile | Gln | Thr | Ile | Lys | Ser | Lys | Ser | Lys | Asp | Gly | Arg | Pro | Leu |      |
|    |     |     |     |     | 250 |     |     |     |     | 255 |     |     |     |     | 260 |     |      |
| 5  | cca | gca | agg | gat | aaa | cgc | gcc | tta | aaa | caa | ttt | gaa | gaa | agg | tta | cga | 931  |
|    | Pro | Ala | Arg | Asp | Lys | Arg | Ala | Leu | Lys | Gln | Phe | Glu | Glu | Arg | Leu | Arg |      |
|    |     |     |     | 265 |     |     |     |     | 270 |     |     |     |     | 275 |     |     |      |
|    | aca | ctt | aag | aag | aga | gag | agg | cat | tta | gaa | ttc | att | gaa | aac | agc | tgg | 979  |
|    | Thr | Leu | Lys | Lys | Arg | Glu | Arg | His | Leu | Glu | Phe | Ile | Glu | Asn | Ser | Trp |      |
| 10 |     |     | 280 |     |     |     |     | 285 |     |     |     |     | 290 |     |     |     |      |
|    | tgg | aca | aaa | ţtt | tgt | ggc | gct | ctg | cgt | ccc | ctg | aag | atc | gtc | tgg | gga | 1027 |
|    | Trp | Thr | Lys | Phe | Cys | Gly | Ala | Leu | Arg | Pro | Leu | Lys | Ile | Val | Trp | Gly |      |
|    |     | 295 |     |     |     |     | 300 |     |     |     |     | 305 |     |     |     |     |      |
|    | ata | ttt | ttc | atc | tta | gtt | gca | ttg | ctg | ttt | gta | att | tct | ctc | ttc | ttg | 1075 |
| 15 | Ile | Phe | Phe | Ile | Leu | Val | Ala | Leu | Leu | Phe | Val | Ile | Ser | Leu | Phe | Leu |      |
|    | 310 |     |     |     |     | 315 | ,   |     |     |     | 320 |     |     |     |     | 325 |      |
|    | tca | aat | tta | gat | aaa | gct | ctt | cat | tca | gct | gga | ata | gat | tct | ggt | ttc | 1123 |
|    | Ser | Asn | Leu | Asp | Lys | Ala | Leu | His | Ser | Ala | Gly | Ile | Asp | Ser | Gly | Phe |      |
|    |     |     |     |     | 330 |     |     |     |     | 335 |     |     |     |     | 340 |     |      |
| 20 | ata | att | ttt | gga | gct | aac | ctg | agt | aat | cca | ctg | aat | atg | ctt | ttg | cct | 1171 |
|    | Ile | Ile | Phe | Gly | Ala | Asn | Leu | Ser | Asn | Pro | Leu | Asn | Met | Leu | Leu | Pro |      |
|    |     |     |     | 345 |     |     |     |     | 350 |     |     |     |     | 355 |     |     |      |
|    | tta | cta | caa | aca | gtt | ttc | cct | ctt | gat | tat | att | ctt | ata | aca | att | att | 1219 |
|    | Leu | Leu | Gln | Thr | Val | Phe | Pro | Leu | Asp | Tyr | Ile | Leu | Ile | Thr | Ile | Ile |      |
| 25 |     |     | 360 |     |     |     |     | 365 |     |     |     |     | 370 |     |     |     |      |

|    | att | atg | tac | ttt | att | ttt | act | tca | atg | gca | gga | att | cga | aat | att | ggc | 1267 |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|    | Ile | Met | Tyr | Phe | Ile | Phe | Thr | Ser | Met | Ala | Gly | Ile | Arg | Asn | Ile | Gly |      |
|    |     | 375 |     |     |     |     | 380 |     |     |     |     | 385 |     |     |     |     |      |
|    | ata | tgg | ttc | ttt | tgg | att | aga | tta | tat | aaa | atc | aga | aga | ggt | aga | acc | 1315 |
| 5  | Ile | Trp | Phe | Phe | Trp | Ile | Arg | Leu | Tyr | Lys | Ile | Arg | Arg | Gly | Arg | Thr |      |
|    | 390 |     |     |     |     | 395 |     |     |     |     | 400 |     |     |     |     | 405 |      |
|    | agg | ccc | caa | gca | ctc | ctt | ttt | ctc | tgc | atg | ata | ctt | ctg | ctt | att | gtc | 1363 |
|    | Arg | Pro | Gln | Ala | Leu | Leu | Phe | Leu | Cys | Met | Ile | Leu | Leu | Leu | Ile | Val |      |
|    |     |     |     |     | 410 |     |     |     |     | 415 |     |     |     |     | 420 |     |      |
| 10 | ctt | cac | act | agc | tac | atg | att | tat | agt | ctt | gct | ccc | caa | tat | gtt | atg | 1411 |
|    | Leu | His | Thr | Ser | Tyr | Met | Ile | Tyr | Ser | Leu | Ala | Pro | Gln | Tyr | Val | Met |      |
|    |     |     |     | 425 |     |     |     |     | 430 |     |     |     |     | 435 |     |     |      |
|    | tat | gga | agc | caa | aat | tac | tta | ata | gag | act | aat | ata | act | tct | gat | aat | 1459 |
|    | Tyr | Gly | Ser | Gln | Asn | Tyr | Leu | Ile | Glu | Thr | Asn | Ile | Thr | Ser | Asp | Asn |      |
| 15 |     |     | 440 |     |     |     |     | 445 |     |     |     |     | 450 |     |     |     |      |
|    | cat | aaa | ggc | aat | tca | acc | ctt | tct | gtg | cca | aag | aga | tgt | gat | gca | gat | 1507 |
|    | His | Lys | Gly | Asn | Ser | Thr | Leu | Ser | Val | Pro | Lys | Arg | Cys | Asp | Ala | Asp |      |
|    |     | 455 |     |     |     |     | 460 |     |     |     |     | 465 |     | ,   |     |     |      |
|    | gct | cct | gaa | gat | cag | tgt | act | gtt | acc | cgg | aca | tac | cta | ttc | ctt | cac | 1555 |
| 20 | Ala | Pro | Glu | Asp | Gln | Cys | Thr | Val | Thr | Arg | Thr | Tyr | Leu | Phe | Leu | His |      |
|    | 470 |     |     |     |     | 475 |     |     |     |     | 480 |     |     |     |     | 485 |      |
|    | aag | ttc | tgg | ttc | ttc | agt | gct | gct | tac | tat | ttt | ggt | aac | tgg | gcc | ttt | 1603 |
|    | Lys | Phe | Trp | Phe | Phe | Ser | Ala | Ala | Tyr | Tyr | Phe | Gly | Asn | Trp | Ala | Phe |      |
|    |     |     |     |     | 490 |     |     |     |     | 495 |     |     |     |     | 500 |     |      |
| 25 | ctt | ggg | gta | ttt | ttg | att | gga | tta | att | gta | tcc | tgt | tgt | aaa | ggg | aag | 1651 |

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Leu Gly Val Phe Leu Ile Gly Leu Ile Val Ser Cys Cys Lys Gly Lys 505 510 515 aaa tog gtt att gaa gga gta gat gaa gat toa gac ata agt gat gat 1699 Lys Ser Val Ile Glu Gly Val Asp Glu Asp Ser Asp Ile Ser Asp Asp 5 520 525 530 gag ccc tct gtc tat tct gct tgacagcctt ctgtcttaaa ggttttataa 1750 Glu Pro Ser Val Tyr Ser Ala 535 540 tgctgactga atatctgtta tgcattttta aagtattaaa ctaacattag gatttgctaa 1810 10 ctagctttca tcaaaaatgg gagcatggct ataagacaac tatattttat tatatgtttt 1870 ctgaagtaac attgtatcat agattaacat tttaaattac cataatcatg ctatgtaaat 1930 ataagactac tggctttgtg agggaatgtt tgtgcaaaat tttttcctct aatgtataat 1990 agtgttaaat tgattaaaaa tcttccagaa ttaatattcc cttttgtcac tttttgaaaa 2050 cataataaat catctgtatc tgtg 2074 15 <210> 28 <211> 2252 <212> DNA <213> Homo sapiens 20 <220> <221> CDS <222> (12)..(1340) <400> 28 gggcgggggc c atg gcg ctg cca tcc cga atc ctg ctt tgg aaa ctt gtg 50

Met Ala Leu Pro Ser Arg Ile Leu Leu Trp Lys Leu Val

25

|   |    |     | 1   |     |     |     |     |     | ţ   | 5   |     |     |     |     |     |     |       |     |
|---|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------|-----|
|   |    | ctt | ctg | cag | agc | tct | gct | gtt | ctc | ctg | cac | tca | ggg | tcc | tcg | gta | ccc   | 98  |
|   |    | Leu | Leu | Gln | Ser | Ser | Ala | Val | Leu | Leu | His | Ser | Gly | Ser | Ser | Val | Pro   |     |
|   |    |     | 15  |     |     |     |     | 20  |     |     |     |     | 25  |     |     |     |       |     |
|   | 5  | gcc | gct | gct | ggc | agc | tcc | gtg | gtg | tcc | gag | tcc | gcg | gtg | agc | tgg | gag   | 146 |
|   |    | Ala | Ala | Ala | Gly | Ser | Ser | Val | Val | Ser | Glu | Ser | Ala | Val | Ser | Trp | Glu   |     |
|   |    | 30  |     |     |     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45    |     |
|   |    | gcg | ggc | gcc | cgg | gcg | gtg | ctg | cgc | tgc | cag | agc | ccg | cgc | atg | gtg | tgg   | 194 |
|   |    | Ala | Gly | Ala | Arg | Ala | Val | Leu | Arg | Cys | Gln | Ser | Pro | Arg | Met | Val | Trp   |     |
| • | 10 |     |     |     |     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |       |     |
|   |    | acc | cag | gac | cgg | ctg | cac | gaç | cgc | cag | cgc | gtg | ctc | cac | tgg | gac | ctg   | 242 |
|   |    | Thr | Gln | Asp | Arg | Leu | His | Asp | Arg | Gln | Arg | Val | Leu | His | Trp | Asp | Leu   |     |
|   |    |     |     |     | 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |       |     |
|   |    | cgc | ggc | ccc | ggg | ggt | ggc | ccc | gcg | cgg | cgc | ctg | ctg | gac | ttg | tac | tcg   | 290 |
|   | 15 | Arg | Gly | Pro | Gly | Gly | Gly | Pro | Ala | Arg | Arg | Leu | Leu | Asp | Leu | Tyr | Ser   |     |
|   |    |     |     | 80  |     |     |     |     | 85  |     |     |     |     | 90  |     |     |       |     |
|   |    | gcg | ggc | gag | cag | cgc | gtg | tac | gag | gcg | cgg | gac | cgc | ggc | cgc | ctg | gag   | 338 |
|   |    | Ala | Gly | Glu | Gln | Arg | Val | Tyr | Glu | Ala | Arg | Asp | Arg | Gly | Arg | Leu | Glu   |     |
|   |    |     | 95  |     |     |     |     | 100 |     |     |     |     | 105 |     |     |     |       |     |
|   | 20 | ctc | tcg | gcc | tcg | gcc | ttc | gac | gac | ggc | aac | ttc | tcg | ctg | ctc | atc | cgc · | 386 |
|   |    | Leu | Ser | Ala | Ser | Ala | Phe | Asp | Asp | Gly | Asn | Phe | Ser | Leu | Leu | Ile | Arg   |     |
|   |    | 110 |     |     |     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125   |     |
|   |    | gcg | gtg | gag | gag | acg | gac | gcg | ggg | ctg | tac | acc | tgc | aac | ctg | cac | cat . | 434 |
|   |    | Ala | Val | Glu | Glu | Thr | Asp | Ala | Gly | Leu | Tyr | Thr | Суз | Asn | Leu | His | His   |     |
|   | 25 |     |     | •   |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |       |     |

|    | cac | tac | tgc | cac | ctc | tac | gag | agc | ctg | gcc | gtc | cgc | ctg | gag | gtc | acc | 482 |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | His | Tyr | Cys | His | Leu | Tyr | Glu | Ser | Leu | Ala | Val | Arg | Leu | Glu | Val | Thr |     |
|    |     |     |     | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |
|    | gac | ggc | ccc | ccg | gcc | acc | ccc | gcc | tac | tgg | gac | ggc | gag | aag | gag | gtg | 530 |
| 5  | Asp | Gly | Pro | Pro | Ala | Thr | Pro | Ala | Tyr | Trp | Asp | Gly | Glu | Lys | Glu | Val |     |
|    |     |     | 160 |     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     |
|    | ctg | gcg | gtg | gcg | cgc | ggc | gca | ccc | gcg | ctt | ctg | acc | tgc | gtg | aac | cgc | 578 |
|    | Leu | Ala | Val | Ala | Arg | Gly | Ala | Pro | Ala | Leu | Leu | Thr | Cys | Val | Asn | Arg |     |
|    |     | 175 |     |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     |     |
| 10 | ggg | cac | gtg | tgg | acc | gac | cgg | cac | gtg | gag | gag | gct | caa | cag | gtg | gtg | 626 |
|    | Gly | His | Val | Trp | Thr | Asp | Arg | His | Val | Glu | Glu | Ala | Gln | Gln | Val | Val |     |
|    | 190 |     |     |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |
|    | cac | tgg | gac | cgg | cag | ccg | ccc | ggg | gtc | ccg | cac | gac | cgc | gcg | gac | cgc | 674 |
|    | His | Trp | Asp | Arg | Gln | Pro | Pro | Gly | Val | Pro | His | Asp | Arg | Ala | Asp | Arg |     |
| 15 |     |     |     |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |
|    | ctg | ctg | gac | ctc | tac | gcg | tcg | ggc | gag | cgc | cgc | gcc | tac | ggg | ccc | ctt | 722 |
|    | Leu | Leu | Asp | Leu | Tyr | Ala | Ser | Gly | Glu | Arg | Arg | Ala | Tyr | Gly | Pro | Leu |     |
|    |     |     |     | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |
|    | ttt | ctg | cgc | gac | cgc | gtg | gct | gtg | ggc | gcg | gat | gcc | ttt | gag | cgc | ggt | 770 |
| 20 | Phe | Leu | Arg | Asp | Arg | Val | Ala | Val | Gly | Ala | Asp | Ala | Phe | Glu | Arg | Gly |     |
|    |     |     | 240 |     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     |
|    | gac | ttc | tca | ctg | cgt | atc | gag | ccg | ctg | gag | gtc | gcc | gac | gag | ggc | acc | 818 |
|    | Asp | Phe | Ser | Leu | Arg | Ile | Glu | Pro | Leu | Glu | Val | Ala | Asp | Glu | Gly | Thr |     |
|    |     | 255 |     |     |     |     | 260 |     |     |     |     | 265 |     |     |     |     |     |
| 25 | tac | tcc | tgc | cac | ctg | cac | cac | cat | tac | tgt | ggc | ctg | cac | gaa | cgc | cgc | 866 |

|    | Tyr | Ser | Cys | His | Leu | His | His | His | Tyr | Суѕ | Gly | Leu | His | Glu      | Arg | Arg |      |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|----------|-----|-----|------|
|    | 270 |     |     |     |     | 275 |     |     |     |     | 280 |     |     |          |     | 285 |      |
|    | gtc | ttc | cac | ctg | acg | gtc | gcc | gaa | ccc | cac | gcg | gag | ccg | ccc      | ccc | cgg | 914  |
|    | Val | Phe | His | Leu | Thr | Val | Ala | Glu | Pro | His | Ala | Glu | Pro | Pro      | Pro | Arg |      |
| 5  |     |     |     |     | 290 |     |     |     |     | 295 |     |     |     |          | 300 |     |      |
|    | ggc | tct | ccg | ggc | aac | ggc | tcc | agc | cac | agc | ggc | gcc | cca | ggc      | cca | gac | 962  |
|    | Gly | Ser | Pro | Gly | Asn | Gly | Ser | Ser | His | Ser | Gly | Ala | Pro | Gly      | Pro | Asp |      |
|    |     |     |     | 305 |     |     |     |     | 310 |     |     |     |     | 315      |     |     |      |
|    | ccc | aca | ctg | gcg | cgc | ggc | cac | aac | gtc | atc | aat | gtc | atc | gtc      | ccc | gag | 1010 |
| 10 | Pro | Thr | Leu | Ala | Arg | Gly | His | Asn | Val | Ile | Asn | Val | Ile | Val      | Pro | Glu |      |
|    |     |     | 320 |     |     |     |     | 325 |     |     |     |     | 330 |          |     |     |      |
|    | agc | cga | gcc | cac | ttc | ttc | cag | cag | ctg | ggc | tac | gtg | ctg | gcc<br>· | acg | ctg | 1058 |
|    | Ser | Arg | Ala | His | Phe | Phe | Gln | Gln | Leu | Gly | Tyr | Val | Leu | Ala      | Thr | Leu |      |
|    |     | 335 |     |     |     |     | 340 |     |     |     |     | 345 |     |          |     |     |      |
| 15 | ctg | ctc | ttc | atc | ctg | cta | ctg | gtc | act | gtc | ctc | ctg | gcc | gcc      | cgc | agg | 1106 |
|    | Leu | Leu | Phe | Ile | Leu | Leu | Leu | Val | Thr | Val | Leu | Leu | Ala | Ala      | Arg | Arg |      |
|    | 350 |     |     |     |     | 355 |     |     |     |     | 360 |     |     |          |     | 365 |      |
|    | cgc | cgc | gga | ggc | tac | gaa | tac | tcg | gac | cag | aag | tcg | gga | aag      | tca | aag | 1154 |
|    | Arg | Arg | Gly | Gly | Tyr | Glu | Tyr | Ser | Asp | Gln | Lys | Ser | Gly | Lys      | Ser | Lys |      |
| 20 |     |     |     |     | 370 |     |     |     |     | 375 |     | •   |     |          | 380 |     |      |
|    | ggg | aag | gat | gtt | aac | ttg | gcg | gag | ttc | gct | gtg | gct | gca | ggg      | gac | cag | 1202 |
|    | Gly | Lys | Asp | Val | Asn | Leu | Ala | Glu | Phe | Ala | Val | Ala | Ala | Gly      | Asp | Gln |      |
|    |     |     |     | 385 |     |     |     | •   | 390 |     |     |     |     | 395      |     |     |      |
|    | atg | ctt | tac | agg | agt | gag | gac | atc | cag | cta | gat | tac | aaa | aac      | aac | atc | 1250 |
| 25 | Met | Leu | Tyr | Arg | Ser | Glu | Asp | Ile | Gln | Leu | Asp | Tyr | Lys | Asn      | Asn | Ile |      |

|    | 40         | 00           | 405        |             | 410          |                |            |
|----|------------|--------------|------------|-------------|--------------|----------------|------------|
| •  | ctg aag ga | ng agg gcg g | ag ctg gcc | cac agc ccc | ctg cct gcc  | aag tac 129    | 98         |
|    | Leu Lys Gl | u Arg Ala G  | lu Leu Ala | His Ser Pro | Leu Pro Ala  | Lys Tyr        |            |
|    | 415        |              | 420        |             | 425          |                |            |
| 5  | atc gac ct | a gac aaa g  | gg ttc cgg | aag gag aac | tgc aaa tag  | ggaggcc 134    | 47         |
|    | Ile Asp Le | eu Asp Lys G | Ly Phe Arg | Lys Glu Asn | Cys Lys      |                |            |
|    | 430        | 4:           | 35         | 440         |              |                |            |
|    | ctgggctcct | ggctgggcca   | gcagctgcac | ctctcctgtc  | tgtgctcctc   | ggggcatctc 140 | )7         |
|    | ctgatgctcc | ggggctcacc   | ccccttccag | cggctggtcc  | cgctttcctg   | gaatttggcc 146 | 57         |
| 10 | tgggcgtatg | cagaggccgc   | ctccacaccc | ctccccagg   | ggcttggtgg   | cagcatagec 152 | 27         |
|    | cccacccctg | cggcctttgc   | tcacgggtgg | ccctgcccac  | ccctggcaca a | accaaaatcc 158 | 37         |
|    | cactgatgcc | catcatgccc   | tcagaccctt | ctgggctctg  | cccgctgggg ( | gcctgaagac 164 | 17         |
|    | attcctggag | gacactccca   | tcagaacctg | gcagccccaa  | aactggggtc a | agcctcaggg 170 | )7         |
|    | caggagtccc | actcctccag   | ggctctgctc | gtccggggct  | gggagatgtt ( | ectggaggag 176 | 57         |
| 15 | gacactccca | tcagaacttg   | gcagccttga | agttggggtc  | agcctcggca ( | ggagtcccac 182 | ?7         |
|    | tecteetggg | gtgctgcctg   | ccaccaagag | ctccccacc   | tgtaccacca 1 | gtgggactc.188  | 37         |
|    | caggcaccat | ctgttctccc   | cagggacctg | ctgacttgaa  | tgccagccct t | gctcctctg 194  | 17         |
|    | tgttgctttg | ggccacctgg   | ggctgcaccc | cctgcccttt  | ctctgcccca t | ecctaccct 200  | )7         |
|    | agccttgctc | tcagccacct   | tgatagtcac | tgggctccct  | gtgacttctg a | accctgacac 206 | ; <b>7</b> |
| 20 | ccctcccttg | gactctgcct   | gggctggagt | ctagggctgg  | ggctacattt q | gcttctgta 212  | :7         |
|    | ctggctgagg | acaggggagg   | gagtgaagtt | ggtttggggt  | ggcctgtgtt o | gccactctca 218 | 17         |
|    |            | tttgcatctg   | ctggtggacc | tgccaccatc  | acaataaagt ( | ecccatctga 224 | 7          |
|    | ttttt      |              |            |             |              | 225            | 2          |

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<211> 1461 <212> DNA <213> Homo sapiens <220> <221> CDS <222> (61)..(849) <400> 29 actegeaggg ceegtggegg tteaggegee agagetggee gateggegtt ggeegeegae 60 atg acg ccc gag gac cca gag gaa acc cag ccg ctt ctg ggg cct cct 10 Met Thr Pro Glu Asp Pro Glu Glu Thr Gln Pro Leu Leu Gly Pro Pro 10 Gly Gly Ser Ala Pro Arg Gly Arg Arg Val Phe Leu Ala Ala Phe Ala 20 25 · 30 15 get gee etg gge eea etc age tte gge tte geg etc gge tac age tee 204 Ala Ala Leu Gly Pro Leu Ser Phe Gly Phe Ala Leu Gly Tyr Ser Ser 35 40 45 ccg gcc atc cct age ctg cag cgc gcc gcg ccc ccg gcc ccg cqc ctg 252 Pro Ala Ile Pro Ser Leu Gln Arg Ala Ala Pro Pro Ala Pro Arg Leu 20 50 55 gac gac gcc gcc tcc tgg ttc ggg gct gtc gtg acc ctg ggt gcc Asp Asp Ala Ala Ala Ser Trp Phe Gly Ala Val Val Thr Leu Gly Ala 65 70 75 80 gcg gcg ggg gga gtg ctg ggc tgg ctg gtg gac cgc gcc ggg cgc 25 Ala Ala Gly Gly Val Leu Gly Gly Trp Leu Val Asp Arg Ala Gly Arg

|    |     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | aag | ctg | agc | ctc | ttg | ctg | tgc | tcc | gtg | ccc | ttc | gtg | gcc | ggc | ttt | gcc | 396 |
|    | Lys | Leu | Ser | Leu | Leu | Leu | Cys | Ser | Val | Pro | Phe | Val | Ala | Gly | Phe | Ala |     |
|    |     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |     |
| 5  | gtc | atc | acc | gcg | gcc | cag | gac | gtg | tgg | atg | ctg | ctg | ggg | ggc | cgc | ctc | 444 |
|    | Val | Ile | Thr | Ala | Ala | Gln | Asp | Val | Trp | Met | Leu | Leu | Gly | Gly | Arg | Leu |     |
|    |     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |     |
|    | ctc | acc | ggc | ctg | gcc | tgc | ggt | gtt | gcc | tcc | cta | gtg | gcc | ccg | gtc | tac | 492 |
|    | Leu | Thr | Gly | Leu | Ala | Cys | Gly | Val | Ala | Ser | Leu | Val | Ala | Pro | Val | Tyr |     |
| 10 |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |     |
|    | atc | tcc | gaa | atc | gcc | tac | cca | gca | gtc | cgg | ggg | ttg | ctc | ggc | tcc | tgt | 540 |
|    | Ile | Ser | Glu | Ile | Ala | Tyr | Pro | Ala | Val | Arg | Gly | Leu | Leu | Gly | Ser | Cys |     |
|    | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |     |
|    | gtg | cag | cta | atg | gtc | gtc | gtc | ggc | atc | ctc | ctg | gcc | tac | ctg | gca | ggc | 588 |
| 15 | Val | Gln | Leu | Met | Val | Val | Val | Gly | Ile | Leu | Leu | Ala | Tyr | Leu | Ala | Gly |     |
|    |     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |     |
|    | tgg | gtg | ctg | gag | tgg | cgc | tgg | ctg | gct | gtg | ctg | ggc | tgc | gtg | ccc | ccc | 636 |
|    | Trp | Val | Leu | Glu | Trp | Arg | Trp | Leu | Ala | Val | Leu | Gly | Cys | Val | Pro | Pro |     |
|    |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |     |
| 20 | tcc | ctc | atg | ctg | ctt | ctc | atg | tgc | ttc | atg | ccc | gag | acc | ccg | cgc | ttc | 684 |
|    | Ser | Leu | Met | Leu | Leu | Leu | Met | Cys | Phe | Met | Pro | Glu | Thr | Pro | Arg | Phe |     |
|    |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |     |
|    | ctg | ctg | act | cag | cac | agg | cgc | cag | gag | gct | gct | cct | ggt | ctt | gtc | agg | 732 |
|    | Leu | Leu | Thr | Gln | His | Arg | Arg | Gln | Glu | Ala | Ala | Pro | Gly | Leu | Val | Arg |     |
| 25 |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |     |

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|    | tgt gg  | t cat  | ggt   | gtt   | cag   | cac   | gag   | tgc   | ctt   | cgg  | cgc   | cta  | ctt   | caa   | gct    | 780  |
|----|---------|--------|-------|-------|-------|-------|-------|-------|-------|------|-------|------|-------|-------|--------|------|
|    | Cys Gly | y His  | Gly   | Val   | Gln   | His   | Glu   | Cys   | Leu   | Arg  | Arg   | Leu  | Leu   | Gln   | Ala    |      |
|    | 225     |        |       |       | 230   |       |       |       |       | 235  |       |      |       |       | 240    |      |
|    | gac cca | a ggg  | tgg   | ccc   | tgg   | caa   | ctc   | ctc   | gca   | cgt  | ggc   | cat  | ctc   | ggc   | gcc    | 828  |
| 5  | Asp Pro | o Gly  | Trp   | Pro   | Trp   | Gln   | Leu   | Leu   | Ala   | Arg  | Gly   | His  | Leu   | Gly   | Ala    |      |
|    |         | •      |       | 245   |       |       |       |       | 250   |      |       |      |       | 255   |        |      |
|    | tgt cto | c tgc  | aca   | gcc   | tgt   | tgat  | tgcca | igc d | gtggg | gcto | gg co | tggc | ctgg  | 2     |        | 876  |
|    | Cys Le  | ı Cys  | Thr   | Ala   | Cys   |       |       |       |       |      |       |      |       |       |        |      |
|    |         |        | 260   |       |       |       |       |       |       |      |       |      |       |       |        |      |
| 10 | cgtggg  | cage a | atgto | cctc  | et to | catc  | gccgg | g agg | gtcct | cag  | gcco  | tato | gga ( | gcctt | ctggc  | 936  |
|    | ttgcctd | ccgc 1 | tttct | gcat  | c ti  | tcagt | gtco  | : ttt | tcac  | ttt  | gtto  | tgtç | gtc ( | cctga | aacta  | 996  |
|    | aaggaaa | agac i | tctgg | jaaca | a at  | tcaca | agcco | att   | ttga  | aggg | gcga  | tgad | cag d | ccact | cacta  | 1056 |
|    | ggggat  | ggag ( | caago | ctgt  | g ad  | eteca | agct  | ggg   | jecea | agc  | ccag  | agco | ccc 1 | tgcct | gccc   | 1116 |
|    | aggggag | gcca ( | gaato | cago  | c c   | cttg  | gagco | : ttg | gtct  | gca  | gggt  | ccct | cc t  | ttcct | gtcat  | 1176 |
| 15 | gctccct | tcca ( | gccca | tgac  | c c   | gggg  | ctagg | g ago | gctca | ctg  | ccto  | ctgt | tc d  | cagct | cctgc  | 1236 |
|    | tgctgct | tctg a | aggac | tcag  | g aa  | acaco | cttcg | ago   | tttç  | gcag | acct  | gcgg | gtc a | agccc | tccat  | 1296 |
|    | gcgcaaq | gact a | aaago | agcg  | g aa  | agag  | gaggt | ggg   | jecto | ctag | gato  | tttg | jtc 1 | ttctg | ıgctgg | 1356 |
|    | aggtgct | tttt   | ggagg | jttgg | g to  | gctg  | ggcat | tca   | igtc  | gctc | ctct  | caco | aca d | gctgc | cttat  | 1416 |
|    | cgggaag | ggaa   | atttg | ıtttg | jc ca | aaata | aaaga | cto   | gacad | caga | aaat  | c    |       |       |        | 1461 |
| 20 |         |        |       |       |       |       |       |       |       |      |       |      |       |       |        |      |
|    | <210> 3 | 30     |       |       |       |       |       |       |       |      |       |      |       |       |        |      |
|    | <211> : | 1122   |       |       |       |       |       |       |       |      |       |      |       |       |        |      |
|    | <212> I | ONA    |       |       |       |       |       |       |       |      |       |      |       |       |        |      |
|    |         |        |       |       |       |       |       |       |       |      |       |      |       |       |        |      |

25 <220>

<213> Homo sapiens

|    | <22  | 1> C  | DS    |       |      |       |       |      |       |      |      |      |       |       |      |        |     |
|----|------|-------|-------|-------|------|-------|-------|------|-------|------|------|------|-------|-------|------|--------|-----|
|    | <222 | 2> (  | 79).  | . (53 | 7)   |       |       |      |       |      |      |      |       |       |      |        |     |
|    | <400 | )> 3( | 0     |       |      | ÷     |       |      |       |      |      |      |       |       |      |        |     |
|    | tgtt | cct   | cgg ( | ggtc  | cgcg | ga go | cgago | ccca | g cto | eteg | gege | gtgi | tegga | agt ( | ctcc | cagccc | 60  |
| 5  | cgcg | ggcco | ccg a | agcg  | cacg | atg   | cgc   | gga  | ccc   | ggg  | cac  | ccc  | ctc   | ctc   | ctg  | ggg    | 111 |
|    |      |       |       |       |      | Met   | Arg   | Gly  | Pro   | Gly  | His  | Pro  | Leu   | Leu   | Leu  | Gly    |     |
|    |      |       |       |       |      | 1     |       |      |       | 5    |      |      |       |       | 10   |        |     |
|    | ctg  | ctg   | ctg   | gtg   | ctg  | ggg   | gcg   | gcg  | ggg   | cgc  | ggc  | cgg  | ggg   | ggc   | gcg  | gag    | 159 |
|    | Leu  | J.eu  | Leu   | Val   | Leu  | Gly   | Ala   | Ala  | Gly   | Arg  | Gly  | Arg  | Gly   | Gly   | Ala  | Glu    |     |
| 10 |      |       |       | 15    |      |       |       |      | 20    |      |      |      |       | 25    |      |        |     |
|    | ccc  | cgg   | gag   | ccg   | gcg  | gac   | gga   | cag  | gcg   | ctg  | ctg  | cgg  | ctg   | gtg   | gtg  | gaa    | 207 |
|    | Pro  | Arg   | Glu   | Pro   | Ala  | Asp   | Gly   | Gln  | Ala   | Leu  | Leu  | Arg  | Leu   | Val   | Val  | Glu    |     |
|    |      |       | 30    |       |      | •     |       | 35   |       |      |      |      | 40    |       |      |        |     |
|    | ctc  | gtc   | cag   | gag   | ctg  | cgg   | aag   | cac  | cac   | tcg  | gcg  | gag  | cac   | aag   | ggc  | ctg    | 255 |
| 15 | Leu  | Val   | Gln   | Glu   | Leu  | Arg   | Lys   | His  | His   | Ser  | Ala  | Glu  | His   | Lys   | Gly  | Leu    |     |
|    |      | 45    |       |       |      |       | 50    |      |       |      |      | 55   |       |       |      |        |     |
|    | cag  | ctc   | ctc   | ggg   | cgg  | gac   | tgc   | gcc  | ctg   | ggc  | cgc  | gcg  | gag   | gcg   | gcg  | ggg    | 303 |
|    | Gln  | Leu   | Leu   | Gly   | Arg  | Asp   | Cys   | Ala  | Leu   | Gly  | Arg  | Ala  | Glu   | Ala   | Ala  | Gly    |     |
|    | 60   |       |       |       |      | 65    |       |      |       |      | 70   |      |       |       |      | 75     |     |
| 20 | ctg  | ggg   | cct   | tcg   | ccg  | gag   | cag   | cga  | gtg   | gaa  | att  | gtt  | cct   | cga   | gat  | ctg    | 351 |
| •  | Leu  | Gly   | Pro   | Ser   | Pro  | Glu   | Gln   | Arg  | Val   | Glu  | Ile  | Val  | Pro   | Arg   | Asp  | Leu    |     |
|    |      |       |       |       | 80   |       |       |      |       | 85   |      |      |       |       | 90   |        |     |
|    | agg  | atg   | aag   | gac   | aag  | ttt   | cta   | aaa  | cac   | ctt  | aca  | ggc  | cct   | ctt   | tat  | ttt    | 399 |
|    | Arg  | Met   | Lys   | Asp   | Lys  | Phe   | Leu   | Lys  | His   | Leu  | Thr  | Gly  | Pro   | Leu   | Tyr  | Phe    |     |
| 25 |      |       |       | 95    |      |       |       |      | 100   |      |      |      |       | 105   |      |        |     |

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|    | agt  | cca   | aag   | tgc   | agc   | aaa   | cac   | ttc   | cat   | aga   | ctt  | tat  | cac   | aac   | acc   | aga    | 447  |
|----|------|-------|-------|-------|-------|-------|-------|-------|-------|-------|------|------|-------|-------|-------|--------|------|
|    | Ser  | Pro   | Lys   | Cys   | Ser   | Lys   | His   | Phe   | His   | Arg   | Leu  | Tyr  | His   | Asn   | Thr   | Arg    |      |
|    |      |       | 110   |       |       |       |       | 115   |       |       |      |      | 120   |       |       |        |      |
|    | gac  | tgc   | acc   | att   | cct   | gca   | tac   | tat   | aaa   | aga   | tgc  | gcc  | agg   | ctt   | ctt   | acc    | 495  |
| 5  | Asp  | Cys   | Thr   | Ile   | Pro   | Ala   | Tyr   | Tyr   | Lys   | Arg   | Cys  | Ala  | Arg   | Leu   | Leu   | Thr    |      |
|    |      | 125   |       |       |       |       | 130   |       |       |       |      | 135  |       |       |       |        |      |
|    | cgg  | ctg   | gct   | gtc   | agt   | cca   | gtg   | tgc   | atg   | gag   | gat  | aag  | cag   | tga   | gcaga | acc    | 544  |
|    | Arg  | Leu   | Ala   | Val   | Ser   | Pro   | Val   | Cys   | Met   | Glu   | Asp  | Lys  | Gln   |       |       |        |      |
|    | 140  |       |       |       |       | 145   |       |       | •     |       | 150  |      |       |       |       |        |      |
| 10 | gtad | cagga | agc a | agcad | cacca | ag ga | agcca | atgag | g aag | gtgco | ttg  | gaaa | accaa | aca ( | gggaa | aacaga | 604  |
|    | acta | tctt  | ta 1  | tacad | catco | cc ct | cate  | ggaca | a aga | agatt | tat  | ttt  | tgcag | gac i | agact | cttcc  | 664  |
|    | ataa | gtec  | ctt t | cgagt | tttc  | gt at | gtto  | gttga | a caç | gtttg | gcag | atat | tatat | tc    | gataa | atcag  | 724  |
|    | tgta | cttg  | jac a | agtgt | tato  | ct gt | cact  | tatt  | taa   | aaaa  | aaa  | acad | caaaa | agg a | aatgo | ctccac | 784  |
|    | attt | gaçç  | gtg t | tagto | gctat | a aa  | acao  | cagaa | a tat | ttca  | attg | tctt | catt  | ag (  | gtgaa | atcgc  | 844  |
| 15 | aaaa | aata  | itt t | cttt  | agaa  | ia ca | ıtaaç | gcaga | ato   | cttaa | agt  | atat | tttc  | cat a | ataac | ataat  | 904  |
|    | ttga | tatt  | ct g  | gtatt | actt  | t ca  | ctgt  | taaa  | tto   | ctcag | gagt | atta | atttg | gga a | acggo | atgaa  | 964  |
|    | aaat | taaa  | at t  | tcgg  | tcat  | g tt  | ttag  | gagad | agt   | ggaç  | rtgt | aaat | ctgt  | .gg ( | ctaat | tctgt  | 1024 |
|    | tggt | cgtt  | tg t  | atta  | ataaa | ıt gt | aaaa  | ıtagt | att   | ccag  | ıcta | ttgt | gcaa  | ata 1 | tgtaa | atagt  | 1084 |
|    | gtaa | ataa  | ac a  | acaag | rtaat | a aa  | itgaa | gtgt  | ttg   | tttt  | :t   |      |       |       |       |        | 1122 |
| 20 |      |       |       |       |       |       |       |       |       |       |      |      |       |       |       |        |      |
|    | <210 | > 31  |       |       |       |       |       |       |       |       |      |      |       |       |       |        |      |

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<212> PRT

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25 <400> 31

|    | Met | Gly | Ala | Ser | Ser | Ser | Ser        | Ala | Leu | Ala | Arg | Leu   | Gly | Leu | Pro | Ala |
|----|-----|-----|-----|-----|-----|-----|------------|-----|-----|-----|-----|-------|-----|-----|-----|-----|
|    | 1   |     |     |     | 5   |     |            |     |     | 10  |     |       |     |     | 15  |     |
|    | Arg | Pro | Trp | Pro | Arg | Trp | Leu        | Gly | Val | Ala | Ala | Leu   | Gly | Leu | Ala | Ala |
|    |     |     |     | 20  |     |     |            |     | 25  |     |     |       |     | 30  |     |     |
| 5  | Val | Ala | Leu | Gly | Thr | Val | Ala        | Trp | Arg | Arg | Ala | Trp   | Pro | Arg | Arg | Arg |
|    |     |     | 35  |     |     |     |            | 40  |     |     |     |       | 45  |     |     |     |
|    | Arg | Arg | Leu | Gln | Gln | Val | Gly        | Thr | Val | Ala | Lys | Leu   | Trp | Ile | Tyr | Pro |
|    |     | 50  |     |     |     |     | 5 <b>5</b> |     |     |     |     | 60    |     |     |     |     |
|    | Val | Lys | Ser | Cys | Lys | Gly | Val        | Pro | Val | Ser | Glu | Ala   | Glu | Cys | Thr | Ala |
| 10 | 65  |     |     |     |     | 70  |            |     |     |     | 75  |       |     |     |     | 80  |
|    | Met | Gly | Leu | Arg | Ser | Gly | Asn        | Leu | Arg | Asp | Arg | Phe   | Trp | Leu | Val | Ile |
|    |     |     |     |     | 85  |     |            |     |     | 90  |     |       |     |     | 95  |     |
|    | Lys | Glu | Asp | Gly | His | Met | Val        | Thr | Ala | Arg | Gln | Glu   | Pro | Arg | Leu | Val |
|    |     |     |     | 100 |     |     |            |     | 105 |     |     |       |     | 110 |     |     |
| 15 | Leu | Ile | Ser | Ile | Ile | Tyr | Glu        | Asn | Asn | Cys | Leu | Ile   | Phe | Arg | Ala | Pro |
|    |     |     | 115 |     |     |     |            | 120 |     |     |     |       | 125 |     |     |     |
|    | Asp | Met | Asp | Gln | Leu | Val | Leu        | Pro | Ser | Lys | Gln | Pro   | Ser | Ser | Asn | Lys |
|    |     | 130 |     |     |     |     | 135        |     |     |     |     | 140   |     |     |     |     |
|    | Leu | His | Asn | Cys | Arg | Ile | Phe        | Gly | Leu | Asp | Ile | Lys   | Gly | Arg | Asp | Cys |
| 20 | 145 |     |     |     |     | 150 |            |     |     |     | 155 |       |     |     |     | 160 |
|    | Gly | Asn | Glu | Ala | Ala | Lys | Trp        | Phe | Thr | Asn | Phe | Leu   | Lys | Thr | Glu | Ala |
|    |     |     |     |     | 165 |     |            |     |     | 170 | ı   |       |     |     | 175 |     |
|    | Tyr | Arg | Leu | Val | Gln | Phe | Glu        | Thr | Asn | Met | Lys | Gly   | Arg | Thr | Ser | Arg |
|    |     |     |     | 180 | ı   |     |            |     | 185 |     |     |       |     | 190 | )   |     |
| 25 | Lys | Leu | Leu | Pro | Thr | Leu | Asp        | Gln | Asn | Phe | Gln | . Val | Ala | Tyr | Pro | Asp |

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Tyr Cys Pro Leu Leu Ile Met Thr Asp Ala Ser Leu Val Asp Leu Asn Thr Arg Met Glu Lys Lys Met Lys Met Glu Asn Phe Arg Pro Asn Ile Val Val Thr Gly Cys Asp Ala Phe Glu Glu Asp Thr Trp Asp Glu Leu Leu Ile Gly Ser Val Glu Val Lys Lys Val Met Ala Cys Pro Arg Cys Ile Leu Thr Thr Val Asp Pro Asp Thr Gly Val Ile Asp Arg Lys Gln Pro Leu Asp Thr Leu Lys Ser Tyr Arg Leu Cys Asp Pro Ser Glu Arg Glu Leu Tyr Lys Leu Ser Pro Leu Phe Gly Ile Tyr Tyr Ser Val Glu Lys Ile Gly Ser Leu Arg Val Gly Asp Pro Val Tyr Arg Met Val <210> 32 <211> 208 <212> PRT <213> Homo sapiens <400> 32 Met Glu Leu Arg Ala Ala Leu Val Leu Val Leu Leu Ile Ala Gly

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|    | Gly | Leu | Phe | Met | Phe | Thr | Tyr | Lys | Ser | Thr | Gln | Phe | Asn | Val | Glu | Gly |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    |     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
|    | Phe | Ala | Leu | Val | Leu | Gly | Ala | Ser | Phe | Ile | Gly | Gly | Ile | Arg | Trp | Thr |
|    |     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
| 5  | Leu | Thr | Gln | Met | Leu | Leu | Gln | Lys | Ala | Glu | Leu | Gly | Leu | Gln | Asn | Pro |
|    |     | 50  |     |     | •   |     | 55  |     |     |     |     | 60  |     |     |     |     |
|    | Ile | Asp | Thr | Met | Phe | His | Leu | Gln | Pro | Leu | Met | Phe | Leu | Gly | Leu | Phe |
|    | 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
|    | Pro | Leu | Phe | Ala | Val | Phe | Glu | Gly | Leu | His | Leu | Ser | Thr | Ser | Glu | Lys |
| 10 |     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
|    | Ile | Phe | Arg | Phe | Gln | Asp | Thr | Gly | Leu | Leu | Leu | Arg | Val | Leu | Gly | Ser |
|    |     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
|    | Leu | Phe | Leu | Gly | Gly | Ile | Leu | Ala | Phe | Gly | Leu | Gly | Phe | Ser | Glu | Phe |
|    |     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
| 15 | Leu | Leu | Val | Ser | Arg | Thr | Ser | Ser | Leu | Thr | Leu | Ser | Ile | Ala | Gly | Ile |
|    |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
|    | Phe | Lys | Glu | Val | Cys | Thr | Leu | Leu | Leu | Ala | Ala | His | Leu | Leu | Gly | Asp |
|    | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
|    | Gln | Ile | Ser | Leu | Leu | Asn | Trp | Leu | Gly | Phe | Ala | Leu | Cys | Leu | Ser | Gly |
| 20 |     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
|    | Ile | Ser | Leu | His | Val | Ala | Leu | Lys | Ala | Leu | His | Ser | Arg | Gly | Asn | Pro |
|    |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
|    | Glu | Ser | Leu | Pro | Glu | Ala | Ser | Val | Phe | Cys | Ser | Ser | Pro | Суз | Asp | Ser |
|    |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 | •   |     |     |

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|    | <210 | <i>&gt;</i> 33 | •    |      |     |     |     |     |                  |     |     |     |     |     |     |     |
|----|------|----------------|------|------|-----|-----|-----|-----|------------------|-----|-----|-----|-----|-----|-----|-----|
|    | <211 | > 40           | 6    |      |     |     |     |     |                  |     |     |     |     |     |     |     |
|    | <212 | > PR           | T    |      |     |     |     |     |                  |     |     |     |     |     |     |     |
|    | <213 | > Ho           | mo s | apie | ens |     |     |     |                  |     |     |     |     |     |     |     |
| 5  | <400 | > 33           | 1    |      |     |     |     |     |                  |     |     |     |     |     |     |     |
|    | Met  | Ala            | Ala  | Gly  | Ala | Gly | Ala | Gly | Ser              | Ala | Pro | Arg | Trp | Leu | Arg | Ala |
|    | 1    |                |      |      | 5   |     |     |     |                  | 10  |     |     |     |     | 15  |     |
|    | Leu  | Ser            | Glu  | Pro  | Leu | Ser | Ala | Ala | Gln              | Leu | Arg | Arg | Leu | Glu | Glu | His |
|    |      |                |      | 20   |     |     |     |     | 25               |     |     |     |     | 30  |     |     |
| 10 | Arg  | Tyr            | Ser  | Ala  | Ala | Gly | Val | Ser | Leu              | Leu | Glu | Pro | Pro | Leu | Gln | Leu |
|    |      |                | 35   |      |     |     |     | 40  |                  |     |     |     | 45  |     |     |     |
|    | Tyr  | Trp            | Thr  | Trp  | Leu | Leu | Gln | Trp | Ile              | Pro | Leu | Trp | Met | Ala | Pro | Asn |
|    |      | 50             |      |      |     |     | 55  |     |                  |     |     | 60  |     |     |     |     |
|    | Ser  | Ile            | Thr  | Leu  | Leu | Gly | Leu | Ala | Val <sub>.</sub> | Asn | ۷al | Val | Thr | Thr | Leu | Val |
| 15 | 65   |                |      |      |     | 70  |     |     |                  |     | 75  |     |     |     |     | 80  |
|    | Leu  | Ile            | Ser  | Tyr  | Cys | Pro | Thr | Ala | Thr              | Glu | Glu | Ala | Pro | Tyr | Trp | Thr |
|    |      |                |      |      | 85  |     |     |     |                  | 90  |     |     |     |     | 95  |     |
|    | Tyr  | Leu            | Leu  | Cys  | Ala | Leu | Gly | Leu | Phe              | Ile | Tyr | Gln | Ser | Leu | Asp | Ala |
|    |      |                |      | 100  |     |     |     |     | 105              |     |     |     |     | 110 | •   | •   |
| 20 | Ile  | Asp            | Gly  | Lys  | Gln | Ala | Arg | Arg | Thr              | Asn | Ser | Cys | Ser | Pro | Leu | Gly |
|    |      |                | 115  |      |     |     |     | 120 |                  |     |     |     | 125 |     |     |     |
|    | Glu  | Leu            | Phe  | Asp  | His | Gly | Cys | Asp | Ser              | Leu | Ser | Thr | Val | Phe | Met | Ala |
|    |      | 130            |      |      |     |     | 135 |     |                  |     |     | 140 |     |     | •   |     |
|    | Val  | Gly            | Ala  | Ser  | Ile | Ala | Ala | Arg | Leu              | Gly | Thr | Tyr | Pro | Asp | Trp | Phe |
| 25 | 145  |                |      |      |     | 150 |     |     |                  |     | 155 |     |     |     |     | 160 |

|    | Phe | Phe | Cys | Ser | Phe | Ile | Gly | Met | Phe | Val  | Phe | Tyr | Cys | Ala | His | Tr  |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|-----|
|    |     |     |     |     | 165 |     |     |     |     | 170  |     |     |     |     | 175 |     |
|    | Gln | Thr | Tyr | Val | Ser | Gly | Met | Leu | Arg | Phe  | Gly | Lys | Val | Asp | Val | Thi |
|    |     |     |     | 180 |     |     |     |     | 185 |      |     |     |     | 190 |     |     |
| 5  | Glu | Ile | Gln | Ile | Ala | Leu | Val | Ile | Val | Phe  | Val | Leu | Ser | Ala | Phe | Gl  |
|    |     |     | 195 |     |     |     |     | 200 |     |      |     |     | 205 |     |     |     |
|    | Gly | Ala | Thr | Met | Trp | Asp | Tyr | Thr | Ile | Pro  | Ile | Leu | Glu | Ile | Lys | Leu |
|    |     | 210 |     |     |     |     | 215 |     |     |      |     | 220 |     |     |     |     |
|    | Lys | Ile | Leu | Pro | Val | Leu | Gly | Phe | Leu | Gly  | Gly | Val | Ile | Phe | Ser | Cys |
| 10 | 225 |     |     |     |     | 230 |     |     |     |      | 235 |     |     |     |     | 240 |
|    | Ser | Asn | Tyr | Phe | His | Val | Ile | Leu | His | Gly  | Gly | Val | Gly | Lys | Asn | Gly |
|    |     |     |     |     | 245 |     |     |     |     | 250  |     |     |     |     | 255 |     |
|    | Ser | Thr | Ile | Ala | Gly | Thr | Ser | Val | Leu | Ser  | Pro | Gly | Leu | His | Ile | Gly |
|    |     |     |     | 260 |     |     |     |     | 265 |      |     |     |     | 270 |     |     |
| 15 | Leu | Ile | Ile | Ile | Leu | Ala | Ile | Met | Ile | Tyr  | Lys | Lys | Ser | Ala | Thr | Asp |
|    |     |     | 275 |     |     |     |     | 280 |     |      |     |     | 285 |     |     |     |
|    | Val | Phe | Glu | Lys | His | Pro | Cys | Leu | Tyr | Ile  | Leu | Met | Phe | Gly | Cys | Val |
|    |     | 290 |     |     |     |     | 295 |     |     |      |     | 300 |     |     |     |     |
|    | Phe | Ala | Lys | Val | Ser | Gln | Lys | Leu | Val | Val  | Ala | His | Met | Thr | Lys | Ser |
| 20 | 305 |     |     |     |     | 310 |     |     |     |      | 315 |     |     |     |     | 320 |
|    | Glu | Leu | Tyr | Leu | Gln | Asp | Thr | Val | Phe | Leu  | Gly | Pro | Gly | Leu | Leu | Phe |
|    |     |     |     |     | 325 |     |     |     |     | 330  |     |     |     |     | 335 |     |
|    | Leu | Asp | Gln | Tyr | Phe | Asn | Asn | Phe | Ile | Asp  | Glu | Tyr | Val | Val | Leu | Trp |
|    |     |     |     | 340 |     |     |     |     | 345 |      |     |     |     | 350 |     |     |
| 25 | Met | Ala | Met | Val | Ile | Ser | Ser | Phe | Asp | ·Met | Val | Tle | ጥህጕ | Phe | Ser | Δla |

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Leu Cys Leu Gln Ile Ser Arg His Leu His Leu Asn Ile Phe Lys Thr Ala Cys His Gln Ala Pro Glu Gln Val Gln Val Leu Ser Ser Lys Ser His Gln Asn Asn Met Asp <210> 34 <211> 618 <212> PRT <213> Homo sapiens <400> 34 Met Glu Val Lys Asn Phe Ala Val Trp Asp Tyr Val Val Phe Ala Ala Leu Phe Phe Ile Ser Ser Gly Ile Gly Val Phe Phe Ala Ile Lys Glu Arg Lys Lys Ala Thr Ser Arg Glu Phe Leu Val Gly Gly Arg Gln Met Ser Phe Gly Pro Val Gly Leu Ser Leu Thr Ala Ser Phe Met Ser Ala Val Thr Val Leu Gly Thr Pro Ser Glu Val Tyr Arg Phe Gly Ala Ser Phe Leu Val Phe Phe Ile Ala Tyr Leu Phe Val Ile Leu Leu Thr Ser 

|    | Glu | Leu | Phe | Leu | Pro | Val | Phe | Tyr | Arg | Ser | Gly | Ile | Thr | Ser | Thr | Туз |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    |     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
|    | Glu | Tyr | Leu | Gln | Leu | Arg | Phe | Asn | Lys | Pro | Val | Arg | Tyr | Ala | Ala | Thi |
|    | •   |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
| 5  | Val | Ile | Tyr | Ile | Val | Gln | Thr | Ile | Leu | Tyr | Thr | Gly | Val | Val | Val | Туз |
|    |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
|    | Ala | Pro | Ala | Leu | Ala | Leu | Asn | Gln | Val | Thr | Gly | Phe | Asp | Leu | Trp | Gl  |
|    | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
|    | Ser | Val | Phe | Ala | Thr | Gly | Ile | Val | Cys | Thr | Phe | Tyr | Cys | Thr | Leu | Gly |
| 10 |     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
|    | Gly | Leu | Lys | Ala | Val | Val | Trp | Thr | Asp | Ala | Phe | Gln | Met | Val | Val | Met |
|    |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
|    | Ile | Val | Gly | Phe | Leu | Thr | Val | Leu | Ile | Gln | Gly | Ser | Thr | His | Ala | Gly |
|    |     |     | 195 |     |     |     | •   | 200 |     |     |     |     | 205 |     |     |     |
| 15 | Gly | Phe | His | Asn | Val | Leu | Glu | Gln | Ser | Thr | Asn | Gly | Ser | Arg | Leu | His |
|    |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
|    | Ile | Phe | Asp | Phe | Asp | Val | Asp | Pro | Leu | Arg | Arg | His | Thr | Phe | Trp | Thr |
|    | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
|    | Ile | Thr | Val | Gly | Gly | Thr | Phe | Thr | Trp | Leu | Gly | Ile | Tyr | Gly | Val | Asn |
| 20 |     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |
|    | Gln | Ser | Thr | Ile | Gln | Arg | Cys | Ile | Ser | Cys | Lys | Thr | Glu | Lys | His | Ala |
|    |     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |
|    | Lys | Leu | Ala | Leu | Tyr | Phe | Asn | Leu | Leu | Gly | Leu | Trp | Ile | Ile | Leu | Val |
|    |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |
| 25 | Cys | Ala | Val | Phe | Ser | Gly | Leu | Ile | Met | Tvr | Ser | His | Phe | Ľvs | asA | Cvs |

|    |     | 290      |     |     |     |     | 295 |     |       |     |     | 300 |     |     |       |       |
|----|-----|----------|-----|-----|-----|-----|-----|-----|-------|-----|-----|-----|-----|-----|-------|-------|
|    | Asp | Pro      | Trp | Thr | Ser | Gly | Ile | Ile | Ser   | Ala | Pro | Asp | Gln | Leu | Met   | Pro   |
|    | 305 |          |     |     |     | 310 |     |     |       |     | 315 |     |     |     |       | 320   |
|    | Tyr | Phe      | Val | Met | Glu | Ile | Phe | Ala | Thr   | Met | Pro | Gly | Leu | Pro | Gly   | Leu   |
| 5  |     |          |     |     | 325 |     |     |     |       | 330 |     |     |     |     | 335   |       |
|    | Phe | Val      | Ala | Cys | Ala | Phe | Ser | Gly | Thr   | Leu | Ser | Thr | Val | Ala | Ser   | Ser   |
|    |     |          |     | 340 |     |     | •   |     | 345   |     |     |     |     | 350 |       |       |
|    | Ile | Asn      | Ala | Leu | Ala | Thr | Val | Thr | Phe   | Glu | Asp | Phe | Val | Lys | Ser   | Cys   |
|    |     |          | 355 |     |     |     |     | 360 |       |     |     |     | 365 |     |       |       |
| 10 | Phe | Pro      | His | Leu | Ser | Asp | Lys | Leu | Ser   | Thr | Trp | Ile | Ser | Ĺys | Gly   | Leu   |
|    |     | 370      |     |     |     |     | 375 |     |       |     |     | 380 |     |     | •     |       |
|    | Cys | Leu      | Leu | Phe | Gly | Val | Met | Cys | Thr   | Ser | Met | Ala | Val | Ala | Ala   | Ser   |
|    | 385 |          |     |     |     | 390 |     |     |       |     | 395 |     |     |     |       | 400   |
|    | Val | Met      | Gly | Gly | Val | Val | Gln | Ala | Ser   | Leu | Ser | Ile | His | Gly | Met   | Cys   |
| 15 |     |          |     |     | 405 |     |     |     |       | 410 |     |     |     |     | 415   |       |
|    | Gly | Gly      | Pro | Met | Leu | Gly | Leu | Phe | Ser   | Leu | Gly | Ile | Val | Phe | Pro   | Phe   |
|    |     |          |     | 420 |     |     |     |     | 425   |     |     |     |     | 430 | •     |       |
|    | Val | Asn      | Trp | Lys | Gly | Ala | Leu | Gly | Gly   | Leu | Leu | Thr | Gly | Ile | Thr   | Leu   |
|    |     |          | 435 |     |     |     |     | 440 | 1     |     |     |     | 445 |     |       |       |
| 20 | Ser | Phe      | Trp | Val | Ala | Ile | Gly | Ala | Phe   | Ile | Tyr | Pro | Ala | Pro | Ala   | Ser   |
|    |     | 450      |     |     |     |     | 455 |     |       |     |     | 460 | ı   |     |       |       |
|    | Lys | Thr      | Trp | Pro | Leu | Pro | Leu | Ser | Thr   | Asp | Gln | Cys | Ile | Lys | s Ser | Asn   |
|    | 465 | <b>i</b> |     |     |     | 470 | ı   |     |       |     | 475 | •   |     |     |       | 480   |
|    | Val | Thr      | Ala | Thr | Gly | Pro | Pro | Val | . Leu | Ser | Ser | Arg | Pro | Gly | / Ile | . Ala |
| 25 |     |          |     |     | 485 |     |     |     |       | 490 | )   |     |     |     | 495   | i     |

|    | Asp | Thr  | Trp | Tyr  | Ser | Ile | Ser | Tyr | Leu | Tyr | Tyr | Ser | Ala | Val | Gly | Cys |
|----|-----|------|-----|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    |     |      |     | 500  |     |     |     |     | 505 |     |     |     |     | 510 |     |     |
|    | Leu | Gly  | Cys | Ile  | Val | Ala | Gly | Val | Ile | Ile | Ser | Leu | Ile | Thr | Gly | Arg |
|    |     |      | 515 |      |     |     |     | 520 |     |     |     |     | 525 |     |     |     |
| 5  | Gln | Arg  | Gly | Glu  | Asp | Ile | Gln | Pro | Leu | Leu | Ile | Arg | Pro | Val | Cys | Asn |
|    |     | 530  |     |      |     |     | 535 |     |     |     |     | 540 |     |     |     |     |
|    | Leu | Phe  | Cys | Phe  | Trp | Ser | Lys | Lys | Tyr | Lys | Thr | Leu | Cys | Trp | Cys | Gly |
|    | 545 |      |     |      |     | 550 |     |     |     |     | 555 |     |     |     |     | 560 |
|    | Val | Gln  | His | Asp  | Ser | Gly | Thr | Glu | Gln | Glu | Asn | Leu | Glu | Asn | Gly | Ser |
| 10 |     |      |     |      | 565 |     |     |     |     | 570 |     |     |     |     | 575 |     |
|    | Ala | Arg  | Lys | Gln  | Gly | Ala | Glu | Ser | Val | Leu | Gln | Asn | Gly | Leu | Arg | Arg |
|    |     |      |     | 580  |     |     |     |     | 585 |     |     |     |     | 590 |     |     |
|    | Glu | Ser  | Leu | Val  | His | Val | Pro | Gly | Tyr | Asp | Pro | Lys | Asp | Lys | Ser | Tyr |
|    |     |      | 595 |      |     |     |     | 600 |     |     |     |     | 605 |     |     |     |
| 15 | Asn | Asn  | Met | Ala  | Phe | Glu | Thr | Thr | His | Phe | •   |     |     |     |     |     |
|    |     | 610  |     |      |     |     | 615 |     |     |     |     |     |     |     |     |     |
|    |     |      |     |      |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <21 | 0> 3 | 5   |      |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <21 | 1> 2 | 08  |      |     |     |     |     |     |     |     |     |     |     |     |     |
| 20 | <21 | 2> P | RT  |      |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <21 | 3> н | ото | sapi | ens |     |     |     |     |     |     |     |     |     |     |     |
|    | <40 | 0> 3 | 5   |      |     |     |     |     |     |     |     |     |     |     |     |     |
|    | Met | Glý  | Leu | Gly  | Ala | Arg | Gly | Ala | Trp | Ala | Ala | Leu | Leu | Leu | Gly | Thr |
|    | 1   |      |     |      | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
| 25 | Leu | Gln  | Val | Leu  | Ala | Leu | Leu | Gly | Ala | Ala | His | Glu | Ser | Ala | Ala | Met |

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|    |     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Ala | Ala | Ser | Ala | Asn | Ile | Glu | Asn | Ser | Gly | Leu | Pro | His | Asn | Ser | Ser |
|    |     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
|    | Ala | Asn | Ser | Thr | Glu | Thr | Leu | Gln | His | Val | Pro | Ser | Asp | His | Thr | Asn |
| 5  |     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
|    | Glu | Thr | Ser | Asn | Ser | Thr | Val | Lys | Pro | Pro | Thr | Ser | Val | Ala | Ser | Asp |
|    | 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
|    | Ser | Ser | Asn | Thr | Thr | ۷al | Thr | Thr | Met | Lys | Pro | Thr | Ala | Ala | Ser | Asn |
|    |     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
| LO | Thr | Thr | Thr | Pro | Gly | Met | Val | Ser | Thr | Asn | Met | Thr | Ser | Thr | Thr | Leu |
|    |     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
|    | Lys | Ser | Thr | Pro | Lys | Thr | Thr | Ser | Val | Ser | Gln | Asn | Thr | Ser | Gln | Ile |
|    |     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
|    | Ser | Thr | Ser | Thr | Met | Thr | Val | Thr | His | Asn | Ser | Ser | Val | Thr | Ser | Ala |
| 15 |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
|    | Ala | Ser | Ser | Val | Thr | Ile | Thr | Thr | Thr | Met | His | Ser | Glu | Ala | Lys | Lys |
|    | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     | •   |     | 160 |
|    | Gly | Ser | Lys | Phe | Asp | Thr | Gly | Ser | Phe | Val | Gly | Gly | Ile | Val | Leu | Thr |
|    |     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
| 20 | Leu | Gly | Val | Leu | Ser | Ile | Leu | Tyr | Ile | Gly | Cys | Lys | Met | Tyr | Tyr | Ser |
|    |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
|    | Arg | Arg | Gly | Ile | Arg | Tyr | Arg | Thr | Ile | Asp | Glu | His | Asp | Ala | Ile | Ile |
|    |     |     | 195 |     |     |     |     | 200 |     |     | ,   |     | 205 |     |     |     |

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|    | <21 | 1> 5  | 02    |      |     |     |     |     |     |     |     |     |     |     |     |     |
|----|-----|-------|-------|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | <21 | 2> PI | RT    |      |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <21 | 3> H  | omo : | sapi | ens |     |     |     |     |     |     |     |     |     |     |     |
|    | <40 | 0> 3  | 6     |      |     |     |     |     |     |     |     |     |     |     |     |     |
| 5  | Met | Ser   | Leu   | Val  | Leu | Leu | Ser | Leu | Ala | Ala | Leu | Cys | Arg | Ser | Ala | Va] |
|    | 1   |       |       |      | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
|    | Pro | Arg   | Glu   | Pro  | Thr | Val | Gln | Cys | Gly | Ser | Glu | Thr | Gly | Pro | Ser | Pro |
|    |     |       |       | 20   |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
|    | Glu | Trp   | Met   | Leu  | Gln | His | Asp | Leu | Ile | Pro | Gly | Asp | Leu | Arg | Asp | Let |
| 10 |     |       | 35    |      |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
|    | Arg | Val   | Glu   | Pro  | Val | Thr | Thr | Ser | Val | Ala | Thr | Gly | Asp | Tyr | Ser | Ile |
|    |     | 50    | ٠     |      |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
|    | Leu | Met   | Asn   | Val  | Ser | Trp | Val | Leu | Arg | Ala | Asp | Ala | Ser | Ile | Arg | Let |
|    | 65  |       |       |      |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
| 15 | Leu | Lys   | Ala   | Thr  | Lys | Ile | Cys | Val | Thr | Gly | Lys | Ser | Asn | Phe | Gln | Sea |
|    |     |       |       |      | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
|    | Tyr | Ser   | Cys   | Val  | Arg | Cys | Asn | Tyr | Thr | Glu | Ala | Phe | Gln | Thr | Gln | Thi |
|    |     |       |       | 100  |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
|    | Arg | Pro   | Ser   | Gly  | Gly | Lys | Trp | Thr | Phe | Ser | Tyr | Ile | Gly | Phe | Pro | Val |
| 20 |     |       | 115   |      |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
|    | Glu | Leu   | Asn   | Thr  | Val | Tyr | Phe | Ile | Gly | Ala | His | Asn | Ile | Pro | Asn | Ala |
|    |     | 130   |       |      |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
|    | Asn | Met   | Asn   | Glu  | Asp | Gly | Pro | Ser | Met | Ser | Val | Asn | Phe | Thr | Ser | Pro |
|    | 145 |       |       |      |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
| 25 | Gly | Cys   | Leu   | Asp  | His | Ile | Met | Lys | Tyr | Lvs | Lvs | Lvs | Cys | Val | Lys | Ala |

|    |     |       |     |       | 165 |     |       |     |     | 170      |      |       |       |          | 175 |     |
|----|-----|-------|-----|-------|-----|-----|-------|-----|-----|----------|------|-------|-------|----------|-----|-----|
|    | Gly | Ser   | Leu | Trp   | Asp | Pro | Asn   | Ile | Thr | Ala      | Cys  | Lys   | Lys   | Asn      | Glu | Glu |
|    |     |       |     | 180   |     |     |       |     | 185 |          |      |       |       | 190      |     |     |
|    | Thr | Val   | Glu | Val   | Asn | Phe | Thr   | Thr | Thr | Pro      | Leu  | Gly   | Asn   | Arg      | Tyr | Met |
| 5  |     |       | 195 |       |     |     |       | 200 |     |          |      |       | 205   |          |     |     |
|    | Ala | Leu   | Ile | Gln   | His | Ser | Thr   | Ile | Ile | Gly      | Phe  | Ser   | Gln   | Val      | Phe | Glu |
|    |     | 210   |     |       |     |     | 215   |     |     |          |      | 220   |       |          |     |     |
|    | Pro | His   | Gln | Lys   | Lys | Gln | Thr   | Arg | Ala | Ser      | Val  | Val   | Ile   | Pro      | Val | Thr |
|    | 225 |       |     |       |     | 230 |       |     |     |          | 235  |       |       |          |     | 240 |
| 10 | Gly | Asp   | Ser | Glu   | Gly | Ala | Thr   | Val | Gln | Leu      | Thr  | Pro   | Tyr   | Phe      | Pro | Thr |
|    |     |       |     |       | 245 |     |       |     |     | 250      |      |       |       |          | 255 |     |
|    | Cys | Gly   | Ser | Asp   | Cys | Ile | Arg   | His | Lys | Gly      | Thr  | Val   | Val   | Leu      | Cys | Pro |
|    |     |       |     | 260   |     |     |       |     | 265 |          |      |       |       | 270      |     |     |
|    | Gln | Thr   | Gly | Val   | Pro | Phe | Pro   | Leu | Asp | Asn      | Asn  | Lys   | Ser   | Lys      | Pro | Gly |
| 15 |     |       | 275 |       |     |     |       | 280 |     |          |      |       | 285   |          |     |     |
|    | Gly | Trp   | Leu | Pro   | Leu | Leu | Leu   | Leu | Ser | Leu      | Leu  | Val   | Ala   | Thr      | Trp | Val |
|    |     | 290   |     |       |     |     | 295   | •   |     |          |      | 300   |       |          |     |     |
|    | Leu | Val   | Ala | Gly   | Ile | Tyr | Leu   | Met | Trp | Arg      | His  | Glu   | Arg   | Ile      | Lys | Lys |
|    | 305 |       |     |       |     | 310 | ı     |     |     |          | 315  |       |       |          |     | 320 |
| 20 | Thr | Ser   | Phe | Ser   | Thr | Thr | Thr   | Leu | Leu | Pro      | Pro  | Ile   | Lys   | Val      | Leu | Val |
|    |     |       |     |       | 325 |     |       |     |     | 330      |      |       |       |          | 335 |     |
|    | Val | Tyr   | Pro | Ser   | Glu | Ile | Cys   | Phe | His | His      | Thr  | Ile   | Cys   | Tyr      | Phe | Thr |
|    |     |       |     | 340   | )   |     |       |     | 345 | <b>;</b> |      |       |       | 350      |     |     |
|    | Glu | . Phe | Leu | ı Glr | Asn | His | S Cys | Arg | Ser | Glu      | \Val | . Ile | e Leu | Glu      | Lys | Trp |
| 25 |     |       | 355 | 5     |     |     |       | 360 | )   |          |      |       | 365   | <b>,</b> |     |     |

|    | Gln  | Lys   | Lys   | Lys   | Ile | Ala | Glu | Met | Gly | Pro | Val | Gln | Trp | Leu | Ala | Thr |
|----|------|-------|-------|-------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    |      | 370   |       |       |     |     | 375 |     |     |     |     | 380 |     |     |     |     |
|    | Gln  | Lys   | Lys   | Ala   | Ala | Asp | Lys | Val | Val | Phe | Leu | Leu | Ser | Asn | Asp | Val |
|    | 385  |       |       |       |     | 390 |     |     |     |     | 395 |     |     |     |     | 400 |
| 5  | Asn  | Ser   | Val   | Cys   | Asp | Gly | Thr | Cys | Gly | Lys | Ser | Glu | Gly | Ser | Pro | Ser |
|    |      |       |       |       | 405 |     |     |     |     | 410 |     |     |     |     | 415 |     |
|    | Glu  | Asn   | Ser   | Gln   | Asp | Leu | Phe | Pro | Leu | Ala | Phe | Asn | Leu | Phe | Cys | Ser |
|    |      |       |       | 420   |     |     |     |     | 425 |     |     |     |     | 430 |     |     |
|    | Asp  | Leu   | Arg   | Ser   | Gln | Ile | His | Leu | His | Lys | Tyr | Val | Val | Val | Tyr | Phe |
| 10 |      |       | 435   |       |     |     |     | 440 |     |     |     |     | 445 |     |     |     |
|    | Arg  | Glu   | Ile   | Asp   | Thr | Lys | Asp | Asp | Tyr | Asn | Ala | Leu | Ser | Val | Cys | Pro |
|    |      | 450   |       |       |     |     | 455 |     |     |     |     | 460 |     |     |     |     |
|    | Lys  | Tyr   | His   | Leu   | Met | Lys | Asp | Ala | Thr | Ala | Phe | Cys | Ala | Glu | Leu | Leu |
|    | 465  |       |       |       |     | 470 |     |     |     |     | 475 |     |     |     |     | 480 |
| 15 | His  | Val   | Lys   | Gln   | Gln | Val | Ser | Ala | Gly | Lys | Arg | Ser | Gln | Ala | Cys | His |
|    |      |       |       |       | 485 |     |     |     |     | 490 |     |     |     |     | 495 |     |
|    | Asp  | Gly   | Cys   | Cys   | Ser | Leu |     |     |     |     |     |     |     |     |     |     |
|    |      |       |       | 500   |     |     |     |     |     |     |     |     |     |     |     |     |
|    |      |       |       |       |     |     |     |     |     |     |     |     |     |     |     |     |
| 20 | <21  | 0> 3  | 7     |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <21  | 1> 33 | 36    |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <21  | 2> PI | RT    |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <21: | 3> H  | omo : | sapie | ens |     |     |     |     |     |     | •   |     |     |     |     |
|    | <400 | 0> 3  | 7     |       |     |     |     |     |     |     |     |     |     |     |     |     |
| 25 | Met  | Arg   | Ala   | Pro   | Ser | Met | Asp | Arg | Ala | Ala | Val | Ala | Arg | Val | Gly | Ala |

|    | 1        |      |      |      | 5   |      |      |      |      | . 10 |      |      |     |     | 15  |      |
|----|----------|------|------|------|-----|------|------|------|------|------|------|------|-----|-----|-----|------|
|    | Val      | Ala  | Ser  | Ala  | Ser | Val  | Cys  | Ala  | Leu  | Val  | Ala  | Gly  | Val | Val | Leu | Ala  |
|    |          |      |      | 20   |     |      |      |      | 25   |      |      |      |     | 30  |     |      |
|    | Gln      | Tyr  | Ile  | Phe  | Thr | Leu  | Lys  | Arg  | Lys  | Thr  | Gly  | Arg  | Lys | Thr | Lys | Ile  |
| 5  |          |      | 35   |      |     |      |      | 40   |      |      |      |      | 45  |     |     |      |
|    | Ile      | Glu  | Met  | Met  | Pro | Glu  | Phe  | Gln  | Lvs  | Ser  | Ser  | Val  | Arg | Ile | Lvs | Asn  |
|    |          | 50   |      |      |     |      | 55   |      | •    |      |      | 60   |     |     |     |      |
|    | Dro      |      | 7.~~ | 17-1 | C1  | C1   |      | Tla  | C    | C1   | T a  |      | T   | C1  | C1  | 71-  |
|    |          | TIIT | Arg  | Val  | GIU |      | TTE  | TTE  | cys  | стА  |      | 116  | ήλε | сту | GTÀ |      |
|    | 65       |      |      |      |     | 70   |      |      |      |      | 75   |      |     |     |     | 80   |
| 10 | Ala      | Lys  | Leu  | Gln  | Ile | Ile  | Thr  | Asp  | Phe  | Asp  | Met  | Thr  | Leu | Ser | Arg | Phe  |
|    |          |      |      |      | 85  |      |      |      |      | 90   |      |      |     |     | 95  |      |
| •  | Ser      | Tyr  | Lys  | Gly  | Lys | Arg  | Cys  | Pro  | Thr  | Cys  | His  | Asn  | Ile | Ile | Asp | Asn  |
|    |          |      |      | 100  |     |      |      |      | 105  |      |      |      |     | 110 |     |      |
|    | Cys      | Lys  | Leu  | Val  | Thr | Asp  | Glu  | Cys  | Arg  | Lys  | Lys  | Leu  | Leu | Gln | Leu | Lys  |
| 15 |          |      | 115  |      |     |      |      | 120  |      |      |      |      | 125 |     |     |      |
|    | Glu      | Lys  | Tyr  | Tyr  | Ala | Ile  | Glu  | Val  | Asp  | Pro  | Val  | Leu  | Thr | Val | Glu | Glu  |
|    |          | 130  |      |      |     |      | 135  |      |      |      |      | 140  |     |     |     |      |
|    | Lys      | Tyr  | Prø  | Tyr  | Met | Val  | Glu  | Trp  | Tyr  | Thr  | Lys  | Ser  | His | Gly | Leu | Leu  |
|    | 145      |      |      |      |     | 150  |      |      |      |      | 155  |      |     |     |     | 160  |
| 20 | Val      | Gln  | Gln  | Ala  | Leu | Pro  | Lys  | Ala  | Lvs  | Leu  | Lys  | Glu  | Ile | Val | Ala | Glu  |
|    |          |      |      |      | 165 |      | •    |      | •    | 170  | •    |      |     |     | 175 |      |
|    | Sor      | Asn  | Wal  | Mat  |     | T.ve | C1., | C1++ | Tres |      | 7 cn | Dho  | Dha | Nam |     | 7.00 |
| •  | Ser      | waħ  | vaı  | Met  |     | пуз  | GIU  | GIĀ  |      | GIU  | ASII | FILE | PHE |     | пÃ2 | Leu  |
|    | <u>.</u> |      | 4.0  | 180  |     |      |      |      | 185  |      |      |      |     | 190 |     |      |
|    | Gln      | Gln  | His  | Ser  | Ile | Pro  | Val  | Phe  | Ile  | Phe  | Ser  | Ala  | Gly | Ile | Gly | Asp  |
| 25 |          |      | 195  |      |     |      |      | 200  |      |      |      |      | 205 |     |     |      |

|    | Val  | Leu   | Glu   | Glu   | Val | Ile | Arg | Gln | Ala | Gly | Val | Tyr | His | Pro | Asn | Val |
|----|------|-------|-------|-------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    |      | 210   |       |       |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
|    | Lys  | Val   | Val   | Ser   | Asn | Phe | Met | Asp | Phe | Asp | Glu | Thr | Gly | Val | Leu | Lys |
|    | 225  |       |       |       |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
| 5  | Gly  | Phe   | Lys   | Gly   | Glu | Leu | Ile | His | Val | Phe | Asn | Lys | His | Asp | Gly | Ala |
|    |      |       |       |       | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |
|    | Leu  | Arg   | Asn   | Thr   | Glu | Tyr | Phe | Asn | Gln | Leu | Lys | Asp | Asn | Ser | Asn | Ile |
|    |      |       |       | 260   |     |     |     |     | 265 |     |     |     |     | 270 |     |     |
|    | Ile  | Leu   | Leu   | Gly   | Asp | Ser | Gln | Gly | Asp | Leu | Arg | Met | Ala | Asp | Gly | Val |
| 10 |      |       | 275   |       |     |     |     | 280 |     |     |     |     | 285 |     |     |     |
|    | Ala  | Asn   | Val   | Glu   | His | Ile | Leu | Lys | Ile | Gly | Tyr | Leu | Asn | Asp | Arg | Val |
|    |      | 290   |       |       |     |     | 295 |     |     |     |     | 300 |     |     |     |     |
|    | Asp  | Glu   | Leu   | Leu   | Glu | Lys | Tyr | Met | Asp | Ser | Tyr | Asp | Ile | Val | Leu | Val |
|    | 305  |       |       |       |     | 310 |     |     |     |     | 315 |     | ·   |     |     | 320 |
| 15 | Gln  | Asp   | Glu   | Ser   | Leu | Glu | Val | Ala | Asn | Ser | Ile | Leu | Gln | Lys | Ile | Leu |
|    |      |       |       |       | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |
|    |      |       |       |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <210 | )> 38 | 3     |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <213 | L> 34 | 10    |       |     |     |     |     |     |     |     |     |     |     |     |     |
| 20 | <212 | 2> PF | T     |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <213 | 3> Ho | omo s | sapie | ens |     |     |     |     |     |     |     |     |     |     |     |
|    | <400 | )> 38 | 3     |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | Met  | Glu   | Pro   | Gly   | Arg | Thr | Gln | Ile | Lys | Leu | Asp | Pro | Arg | Tyr | Thr | Ala |
|    | 1    |       |       |       | 5   |     |     | •   |     | 10  |     |     |     |     | 15  |     |
| 25 | Asp  | Leu   | Leu   | Glu   | Val | Leu | Lys | Thr | Asn | Tyr | Gly | Ile | Pro | Ser | Ala | Cys |

|    |     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Phe | Ser | Gln | Pro | Pro | Thr | Ala | Ala | Gln | Leu | Leu | Arg | Ala | Leu | Gly | Pro |
|    |     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
|    | Val | Glu | Leu | Ala | Leu | Thr | Ser | Ile | Leu | Thr | Leu | Leu | Ala | Leu | Gly | Ser |
| 5  |     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
|    | Ile | Ala | Ile | Phe | Leu | Glu | Asp | Ala | Val | Tyr | Leu | Tyr | Lys | Asn | Thr | Leu |
|    | 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
|    | Cys | Pro | Ile | Lys | Arg | Arg | Thr | Leu | Leu | Trp | Lys | Ser | Ser | Ala | Pro | Thr |
|    |     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
| 10 | Val | Val | Ser | Val | Leu | Cys | Cys | Phe | Gly | Leu | Trp | Ile | Pro | Arg | Ser | Leu |
|    |     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
|    | Val | Leu | Val | Glu | Met | Thr | Ile | Thr | Ser | Phe | Tyr | Ala | Val | Cys | Phe | Tyr |
|    |     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
|    | Leu | Leu | Met | Leu | Val | Met | Val | Glu | Gly | Phe | Gly | Gly | Lys | Glu | Ala | Val |
| 15 |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
|    | Leu | Arg | Thr | Leu | Arg | Asp | Thr | Pro | Met | Met | Val | His | Thr | Gly | Pro | Суз |
|    | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
|    | Cys | Cys | Суз | Cys | Pro | Cys | Cys | Pro | Arg | Leu | Leu | Leu | Thr | Arg | Lys | Lys |
|    |     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
| 20 | Leu | Gln | Leu | Leu | Met | Leu | Gly | Pro | Phe | Gln | Tyr | Ala | Phe | Leu | Lys | Ile |
|    |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
|    | Thr | Leu | Thr | Leu | Val | Gly | Leu | Phe | Leu | Ile | Pro | Asp | Gly | Ile | Tyr | Asp |
|    |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
|    | Pro | Ala | Asp | Ile | Ser | Glu | Gly | Ser | Thr | Ala | Leu | Trp | Ile | Asn | Thr | Phe |
| 25 |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |

|    | Leu  | Gly   | Val   | Ser  | Thr | Leu | Leu | Ala | Leu | Trp | Thr      | Leu | Gly | Ile | Ile | Ser |
|----|------|-------|-------|------|-----|-----|-----|-----|-----|-----|----------|-----|-----|-----|-----|-----|
|    | 225  |       |       |      |     | 230 |     | ,   |     |     | 235      |     |     |     |     | 240 |
|    | Arg  | Gln   | Ala   | Arg  | Leu | His | Leu | Gly | Glu | Gln | Asn      | Met | Gly | Ala | Lys | Phe |
|    |      |       |       |      | 245 |     |     |     |     | 250 |          |     |     |     | 255 |     |
| 5  | Ala  | Leu   | Phe   | Gln  | Val | Leu | Leu | Ile | Leu | Thr | Ala      | Leu | Gln | Pro | Ser | Ile |
|    |      |       |       | 260  |     |     |     |     | 265 |     |          |     |     | 270 |     |     |
|    | Phe  | Ser   | Val   | Leu  | Ala | Asn | Gly | Gly | Gln | Ile | Ala      | Cys | Ser | Pro | Pro | Туг |
|    |      |       | 275   |      |     |     |     | 280 | •   |     |          |     | 285 |     |     |     |
|    | Ser  | Ser   | Lys   | Thr  | Arg | Ser | Gln | Val | Met | Asn | Cys<br>· | His | Leu | Leu | Ile | Leu |
| 10 |      | 290   |       |      | •   |     | 295 |     |     |     |          | 300 |     |     |     |     |
|    | Glu  | Thr   | Phe   | Leu  | Met | Thr | Val | Leu | Thr | Arg | Met      | Tyr | Tyr | Arg | Arg | Lys |
|    | 305  |       |       |      |     | 310 |     |     |     |     | 315      |     |     |     |     | 320 |
|    | Asp  | His   | Lys   | Val  | Gly | Tyr | Glu | Thr | Phe | Ser | Ser      | Pro | Asp | Leu | Asp | Leu |
|    |      |       |       |      | 325 |     |     |     |     | 330 |          |     |     |     | 335 |     |
| 15 | Asn  | Leu   | Lys   | Ala  |     |     |     |     |     |     |          |     |     |     |     |     |
|    |      |       |       | 340  |     |     |     |     |     |     |          |     |     |     |     |     |
|    |      |       |       |      |     |     |     |     |     |     |          |     |     |     |     |     |
|    | <210 | O> 39 | 9     |      |     |     |     |     |     |     |          |     |     |     |     |     |
|    | <21  | 1> 22 | 23    |      | ,   |     |     |     |     |     |          |     |     |     |     |     |
| 20 | <212 | 2> PI | RT    |      |     |     |     |     |     |     |          |     |     |     |     |     |
|    | <21  | 3> Ho | omo : | sapi | ens |     |     |     |     |     |          |     |     |     |     |     |
|    | <400 | )> 39 | 9     |      |     |     |     |     |     |     |          |     |     |     |     |     |
|    | Met  | Leu   | Trp   | Arg  | Gln | Leu | Ile | Tyr | Trp | Gln | Leu      | Leu | Ala | Leu | Phe | Phe |
|    | 1    |       |       |      | 5   |     |     |     |     | 10  |          |     |     |     | 15  |     |
| 25 | Leu  | Pro   | Phe   | Cys  | Leu | Cys | Gln | Asp | Glu | Tyr | Met      | Glu | Val | Ser | Glv | Arc |

|     |      |     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
|-----|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|     |      | Thr | Asn | Lys | Val | Val | Ala | Arg | Ile | Val | Gln | Ser | His | Gln | Gln | Thr | Gly |
|     |      |     |     | 35  |     |     |     |     | 40  |     |     |     | ٠   | 45  |     |     |     |
|     |      | Arg | Ser | Gly | Ser | Arg | Arg | Glu | Lys | Val | Arg | Glu | Arg | Ser | His | Pro | Lys |
|     | 5    |     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
|     |      | Thr | Gly | Thr | Val | Asp | Asn | Asn | Thr | Ser | Thr | Asp | Leu | Lys | Ser | Leu | Arg |
|     |      | 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
|     |      | Pro | Asp | Glu | Leu | Pro | His | Pro | Glu | Val | Asp | Asp | Leu | Ala | Gln | Ile | Thr |
|     |      |     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
| 1   | .0   | Thr | Phe | Trp | Gly | Gln | Ser | Pro | Gln | Thr | Gly | Gly | Leu | Pro | Pro | Asp | Cys |
|     |      |     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
|     |      | Ser | Lys | Cys | Cys | His | Gly | Asp | Tyr | Ser | Phe | Arg | Gly | Tyr | Gln | Gly | Pro |
|     |      |     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
|     |      | Pro | Gly | Pro | Pro | Gly | Pro | Pro | Gly | Ile | Pro | Gly | Asn | His | Gly | Asn | Asn |
| . 1 | .5   |     | 130 | •   |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
|     |      | Gly | Asn | Asn | Gly | Ala | Thr | Gly | His | Glu | Gly | Ala | Lys | Gly | Glu | Lys | Gly |
|     |      | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
|     |      | Asp | Lys | Gly | Asp | Leu | Gly | Pro | Arg | Gly | Glu | Arg | Gly | Gln | His | Gly | Pro |
|     |      |     |     |     |     | 165 |     |     |     |     | 170 | •   |     |     |     | 175 |     |
| 2   | :0 · | Lys | Gly | Glu | Lys | Gly | Tyr | Pro | Gly | Ile | Pro | Pro | Glu | Leu | Gln | Ile | Ala |
|     |      |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
|     |      | Phe | Met | Ala | Ser | Leu | Ala | Thr | His | Phe | Ser | Asn | Gln | Asn | Ser | Gly | Ile |
|     |      |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
|     |      | Ile | Phe | Ser | Ser | Val | Glu | Thr | Asn | Ile | Gly | Asn | Phe | Leu | Met | Ser |     |
| 2   | 25   |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |

|    | <21 | 0> 4  | 0     |      |     |     |     |     |     |     |     |     |       |     |     |     |
|----|-----|-------|-------|------|-----|-----|-----|-----|-----|-----|-----|-----|-------|-----|-----|-----|
|    | <21 | 1> 3  | 09    |      |     |     |     |     |     |     |     |     |       |     |     |     |
|    | <21 | 2> PI | RT    |      |     |     |     |     |     |     |     |     |       |     |     |     |
| 5  | <21 | 3> H  | omo : | sapi | ens |     |     |     |     |     |     |     |       |     |     |     |
|    | <40 | 0> 40 | 0     |      |     |     |     |     |     |     |     |     |       |     |     |     |
|    | Met | Ala   | Thr   | Leu  | Ser | Val | Ile | Gly | Ser | Ser | Ser | Leu | Ile   | Ala | Tyr | Ala |
|    | 1   |       |       |      | 5   |     |     |     |     | 10  |     |     |       |     | 15  |     |
|    | Val | Phe   | His   | Asn  | Ile | Gln | Lys | Ser | Pro | Glu | Ile | Arg | Pro   | Leu | Phe | Ty: |
| 10 |     |       |       | 20   |     |     |     |     | 25  |     |     |     |       | 30  |     |     |
|    | Leu | Ser   | Phe   | Cys  | Asp | Leu | Leu | Leu | Gly | Leu | Cys | Trp | Leu   | Thr | Glu | Th: |
|    |     |       | 35    |      |     |     |     | 40  |     |     |     |     | 45    |     |     |     |
|    | Leu | Leu   | Tyr   | Gly  | Ala | Ser | Val | Ala | Asn | Lys | Asp | Ile | Ile   | Cys | Tyr | Ası |
|    |     | 50    |       |      |     |     | 55  |     |     |     |     | 60  |       |     |     |     |
| 15 | Leu | Gln   | Ala   | Val  | Gly | Gln | Ile | Phe | Tyr | Ile | Ser | Ser | Phe   | Leu | Tyr | Tha |
|    | 65  |       |       |      |     | 70  |     |     |     |     | 75  |     |       |     |     | 80  |
|    | Val | Asn   | Tyr   | Ile  | Trp | Tyr | Leu | Tyr | Thr | Glu | Leu | Arg | Met   | Lys | His | Thi |
|    |     |       |       |      | 85  |     |     |     |     | 90  |     |     |       |     | 95  |     |
|    | Gln | Ser   | Gly   | Gln  | Ser | Thr | Ser | Pro | Leu | Val | Ile | Asp | Tyr   | Thr | Cys | Arç |
| 20 |     |       |       | 100  |     |     |     |     | 105 |     |     |     |       | 110 |     |     |
|    | Val | Cys   | Gln   | Met  | Ala | Phe | Val | Phe | Ser | Arg | Cys | Ile | Leu   | Met | His | Sei |
|    |     |       | 115   |      |     |     |     | 120 |     |     |     |     | 125   |     |     |     |
|    | Pro | Pro   | Ser   | Ala  | Met | Ala | Glu | Leu | Pro | Pro | Ser | Ala | Asn   | Thr | Ser | Va] |
|    |     | 130   |       |      |     |     | 135 |     |     |     |     | 140 |       |     |     |     |
| 25 | Cvs | Ser   | Thr   | Leu  | Tvr | Phe | Tvr | Glv | Tle | בומ | Tle | Phe | T.es: | Glv | Sar | Dha |

|    | 145   |      |     |     |           | 150 |      |     |       |     | 155 |     |       |     |     | 160    |
|----|-------|------|-----|-----|-----------|-----|------|-----|-------|-----|-----|-----|-------|-----|-----|--------|
|    | Val   | Leu  | Ser | Leu | Leu       | Thr | Ile  | Met | Val   | Leu | Leu | Ile | Arg   | Ala | Gln | Thr    |
|    |       |      |     |     | 165       |     |      |     |       | 170 |     |     |       |     | 175 |        |
|    | Leu   | Tyr  | Lys | Lys | Phe       | Val | Lys  | Ser | Thr   | Gly | Phe | Leu | Gly   | Ser | Glu | Gln    |
| 5  |       |      |     | 180 |           |     |      |     | 185   |     |     |     |       | 190 |     |        |
|    | Trp   | Ala  | Val | Ile | His       | Ile | Val  | Asp | Gln   | Arg | Val | Arg | Phe   | Tyr | Pro | Val    |
|    |       |      | 195 |     |           |     |      | 200 |       |     |     |     | 205   |     |     |        |
|    | Ala   | Phe  | Phe | Cys | Cvs       | Trp | Glv  | Pro | Ala   | Val | Ile | Leu | Met   | Ile | Ile | Lys    |
|    |       | 210  |     | •   | •         | •   | 215  |     |       |     |     | 220 |       |     |     | •      |
| 10 | T.011 |      | Luc | Pro | Gln       | Δen |      | Lve | T.011 | Hie | Met |     | T.O.1 | Tur | Val | T.e.11 |
| 10 |       | 1111 | Lys | 110 | · · · · · | -   | **** | 2,0 | 200   |     |     |     |       | -1- | ·   | 240    |
|    | 225   |      |     |     |           | 230 |      |     |       |     | 235 |     |       |     |     |        |
|    | Gln   | Ala  | Leu | Thr | Ala       | Thr | Ser  | Gln | Gly   | Leu | Leu | Asn | Cys   | Gly | Val | Tyr    |
|    |       |      |     |     | 245       |     |      |     |       | 250 |     |     |       |     | 255 |        |
|    | Gly   | Trp  | Thr | Gln | His       | Lys | Phe  | His | Gln   | Leu | Lys | Gln | Glu   | Ala | Arg | Arg    |
| 15 |       |      |     | 260 |           |     |      |     | 265   |     |     |     |       | 270 |     |        |
|    | Asp   | Ala  | Asp | Thr | Gln       | Thr | Pro  | Leu | Leu   | Cys | Ser | Gln | Lys   | Arg | Phe | Tyr    |
|    |       |      | 275 |     |           |     |      | 280 |       |     |     |     | 285   |     |     |        |
|    | Ser   | Arg  | Gly | Leu | Asn       | Ser | Leu  | Glu | Ser   | Thr | Leu | Thr | Phe   | Pro | Ala | Ser    |
|    |       | 290  |     |     |           |     | 295  |     |       |     |     | 300 |       |     |     |        |
| 20 | Thr   | Ser  | Thr | Ile | Phe       |     |      |     |       |     |     |     |       |     |     |        |
|    | 305   |      |     |     |           |     |      |     |       |     |     |     |       |     |     |        |
|    |       |      |     |     |           |     |      |     |       | •   |     |     |       |     |     |        |
|    | <21   | 0> 4 | 1   |     |           |     |      |     |       |     |     |     |       |     |     |        |
|    |       |      |     |     |           |     |      |     |       |     |     |     |       |     |     |        |
| ٥٢ |       | 1> 1 |     |     |           |     |      |     |       |     |     |     |       |     |     |        |
| 25 | <21   | 2> D | NA  |     |           |     |      |     |       |     |     |     |       |     |     |        |

### 95 / 346

<213> Homo sapiens .

<400> 41

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<210> 42

<211> 627

<212> DNA

<213> Homo sapiens

25 <400> 42

#### 96/346

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| ttcacctaca | agtccacaca | gttcaacgtg | gagggcttcg | ccttggtgct | gggggcctcg | 120 |
| ttcatcggtg | gcattcgctg | gaccctcacc | cagatgctcc | tgcagaaggc | tgaactcggc | 180 |
| ctccagaatc | ccatcgacac | catgttccac | ctgcagccac | tcatgttcct | ggggctcttc | 240 |
| cctctctttg | ctgtatttga | aggtctccat | ttgtccacat | ctgagaaaat | cttccgtttc | 300 |
| caggacacag | ggctgctcct | gcgggtactt | gggagcctct | tccttggcgg | gattctcgcc | 360 |
| tttggtttgg | gcttctctga | gttcctcctg | gtctccagaa | cctccagcct | cactctctcc | 420 |
| attgccggca | tttttaagga | agtctgcact | ttgctgttgg | cagctcatct | gctgggcgat | 480 |
| cagatcagcc | tcctgaactg | gctgggcttc | gccctctgcc | tctcgggaat | atccctccac | 540 |
| gttgccctca | aagccctgca | ttccagaggt | aacccagagt | cccttccaga | agcctctgtt | 600 |
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<210> 43

15 <211> 1221

5

10

20

25

<212> DNA

<213> Homo sapiens

<400> 43

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#### 97 /346

gtatttatgg cagtgggagc ttcaattgcc gctcgcttag gaacttatcc tgactggttt 480 tttttctgct cttttattgg gatgtttgtg ttttattgcg ctcattggca gacttatgtt 540 tcaggcatgt tgagatttgg aaaagtggat gtaactgaaa ttcagatagc tttagtgatt 600 gtctttgtgt tgtctgcatt tggaggagca acaatgtggg actatacgat tcctattcta 660 5 gaaataaaat tgaagatcct tccagttctt ggatttctag gtggagtaat attttcctgt 720 tcaaattatt tccatgttat cctccatggt ggtgttggca agaatggatc cactatagca 780 ggcaccagtg tettgtcacc tggactccac ataggactaa ttattatact qqcaataatq 840 atctataaaa agtcagcaac tgatgtgttt gaaaagcatc cttgtcttta tatcctaatg 900 tttggatgtg tctttgctaa agtctcacaa aaattagtgg tagctcacat gaccaaaagt 960 10 gaactatatc ttcaagacac tgtctttttg gggccaggtc ttttgttttt agaccagtac 1020 tttaataact ttatagacga atatgttgtt ctatggatgg caatggtgat ttcttcattt 1080 gatatggtga tatactttag tgctttgtgc ctgcaaattt caagacacct tcatctaaat 1140 atattcaaga ctgcatgtca tcaagcacct gaacaggttc aagttctttc ttcaaagagt 1200 catcagaata acatggattg a 1221

15

25

<210> 44

<211> 1857

<212> DNA

<213> Homo sapiens

20 <400> 44

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5

10

15

20

25

#### 98 /346

cctgtgttct acagatctgg tatcaccagc acttatgagt acttacaact acgattcaac 360 aaaccagttc gctatgctgc cacagtcatc tacattgtac agacgattct ctacacagga 420 gtggtggtgt atgctcctgc cctggcactc aatcaagtga ctgggtttga tctctggggc 480 tctgtgtttg caacaggaat tgtttgcaca ttctactgta ccctgggagg attaaaagca 540 gtggtgtgga cagatgcatt tcagatggtt gtcatgattg tgggcttctt aacggttctc 600 attcaaggat caactcatgc tgggggattc cacaatgtat tagagcaatc aacaaatgga 660 tctcgactac atatatttga ctttgatgta gatcctctca ggcgacacac tttttggact 720 atcacagtgg gaggaacttt tacttggctc ggaatctatg gggtcaatca atcaactatt 780 caqcqatqca tctcttqcaa aacagaaaag catgctaagc ttgccttgta ttttaacttg 840 ctqqqtctct ggatcattct ggtgtgtgct gtcttctctg gcttaatcat gtactctcac 900 tttaaagact gtgacccttg gacttctggc atcatctcag caccagacca gctgatgccg 960 tactttgtca tggagatatt tgccacaatg ccaggactgc caggactttt tgtggcttgt 1020 qccttcaqtq qaactctgag caccgtggct tccagcatca atgccttggc aacagtgacc 1080 tttgaggatt ttgtcaagag ctgttttcct catctctccg acaagctgag cacctggatc 1140 agtaaagget tatgtetett atttggegtg atgtgtacet etatggetgt ggetgeatet 1200 gtcatgggag gtgttgtgca ggcttccctc agcattcacg gcatgtgtgg aggaccaatg 1260 ctgggcttat tctccctggg aatcgtgttc ccttttgtga actggaaggg tgcactagga 1320 qqtcttctta ctqqaatcac cttqtcattt tqqqtqqcca ttqqqqqcctt catttaccct 1380 gtgacagcaa cagggcctcc agtactatcc agcagacctg gaatagctga tacctggtac 1500 tegateteet acetttaeta cagtgeagtg ggetgettag gatgeattgt tgctggagta 1560 atcatcagcc tcataacagg tcgccaaaga ggtgaggata ttcaaccact gttaattaga 1620 ccagtttgta atttattttg cttttggtct aagaagtaca aaacactatg ctggtgcgga 1680 gttcagcatg acagtgggac agagcaggaa aaccttgaga atggcagtgc ccggaaacag 1740 ggggctgaat ctgtcttaca gaacggactc agaagagaaa gcctggtaca tgttccaggc 1800

### 99/346

tatgatccta aggacaaaag ctacaacaat atggcatttg agactaccca tttctaa 1857

<210> 45

<211> 627

5 <212> DNA

10

15

<213> Homo sapiens

<400> 45

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20 <210> 46

<211> 1509

<212> DNA

<213> Homo sapiens

<400> 46

25 atgtcgctcg tgctgctaag cctggccgcg ctgtgcagga gcgccgtacc ccgagagccg 60

5

10

15

20

25

#### 100/346

accgttcaat gtggctctga aactgggcca tctccagagt ggatgctaca acatgatcta 120 atccegggag acttgaggga cctccgagta gaacctgtta caactagtgt tgcaacaggg 180 gactattcaa ttttgatgaa tgtaagctgg gtactccggg cagatgccag catccgcttg 240 ttgaaggcca ccaagatttg tgtgacggc aaaagcaact tccagtccta cagctgtgtg 300 ttttcctaca tcggcttccc tgtagagctg aacacagtct atttcattgg ggcccataat 420 attoctaatg caaatatgaa tgaagatggc cottocatgt ctqtqaattt cacctcacca 480 ggctgcctag accacataat gaaatataaa aaaaagtgtg tcaaggccgg aagcctgtgg 540 gatccgaaca tcactgcttg taagaagaat gaggagacag tagaagtgaa cttcacaacc 600 actoccotgg gaaacagata catggotott atocaacaca gcactatoat cggqttttot 660 caggtgtttg agccacacca gaagaaacaa acgcgagctt cagtggtgat tccagtgact 720 ggggatagtg aaggtgctac ggtgcagctg actccatatt ttcctacttg tqqcaqcqac 780 tgcatccgac ataaaggaac agttgtgctc tgcccacaaa caggcqtccc tttccctctg 840 gataacaaca aaagcaagcc gggaggctgg ctqcctctcc tcctqctqtc tctqctqqtq 900 gccacatggg tgctggtggc agggatctat ctaatgtgga ggcacqaaaq qatcaaqaaq 960 acttectttt ctaccaccac actactgeec eccattaagg ttettgtggt ttacccatet 1020 gaaatatgtt tccatcacac aatttgttac ttcactgaat ttcttcaaaa ccattgcaga 1080 agtgaggtca tccttgaaaa gtggcagaaa aagaaaatag cagagatqqq tccaqtqcaq 1140 tggcttgcca ctcaaaagaa ggcagcagac aaagtcgtct tccttctttc caatgacgtc 1200 aacagtgtgt gcgatggtac ctgtggcaag agcgagggca gtcccagtga gaactctcaa 1260 gacctettee ceettgeett taacetttte tgeagtgate taagaageea gatteatetg 1320 cacaaatacg tggtggtcta ctttagagag attgatacaa aagacgatta caatgctctc 1380 agtgtctgcc ccaagtacca cctcatgaag gatgccactg ctttctgtgc agaacttctc 1440 catgtcaagc agcaggtgtc agcaggaaaa agatcacaag cctgccacga tggctgctgc 1500 tccttgtag 1509

#### 101/346

<210> 47

<211> 1011

<212> DNA

5 <213> Homo sapiens

<400> 47

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15

20

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#### 102/346

<211> 1023

<212> DNA

<213> Homo sapiens

<400> 48

5

15

20

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<210> 49

25 <211> 672

#### 103/346

<212> DNA

<213> Homo sapiens

<400> 49

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<210> 50

<211> 930

<212> DNA

20 <213> Homo sapiens

<400> 50

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#### 104/346

gtcaattaca totggtattt gtacacagag ctgaggatga aacacaccca gagtggacag 300
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tcaaggtgta tottgatgca otcaccacca tcagccatgg otgaacttcc accttctgcc 420
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gtactcagcc toottaccat tatggtotta ottatccgag occagacatt gtataagaag 540
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caacgggtgc gottotaccc agtggoottc tittgctgct ggggcccage tgtcattcta 660
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caggototaa oggcaacatc tcagggtota otcaactgtg gagtatatgg otggacgcag 780
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<210> 51

15 <211> 1617

5

10

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

20 <222> (255)..(1262)

<400> 51

25

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|    | gccctcgc | tc tgc | c atg  | ggc  | gct | tcc | agc | tcc | tcc | gcg | ctg | gcc | cgc | CTC | 290 |
|----|----------|--------|--------|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    |          |        | Met    | Gly  | Ala | Ser | Ser | Ser | Ser | Ala | Leu | Ala | Arg | Leu |     |
|    |          |        | 1      |      |     |     | 5   |     |     |     |     | 10  |     |     |     |
|    | ggc ctc  | cca go | c cgg  | ccc  | tgg | ccc | agg | tgg | ctc | ggg | gtc | gcc | gcg | cta | 338 |
| 5  | Gly Leu  | Pro Al | a Arg  | Pro  | Trp | Pro | Arg | Trp | Leu | Gly | Val | Ala | Ala | Leu |     |
|    |          | 15     |        |      |     | 20  |     |     |     |     | 25  |     |     |     |     |
|    | gga ctg  | gcc gc | c gtg  | gcc  | ctg | ggg | act | gtc | gcc | tgg | cgc | cgc | gca | tgg | 386 |
|    | Gly Leu  | Ala Al | a Val  | Ala  | Leu | Gly | Thr | Val | Ala | Trp | Arg | Arg | Ala | Trp |     |
|    | 30       |        |        |      | 35  |     |     |     |     | 40  |     |     |     |     |     |
| 10 | ccc agg  | cgg cg | c cgg  | cgg  | ctg | cag | cag | gtg | ggc | acc | gtg | gcg | aag | ctc | 434 |
|    | Pro Arg  | Arg Ar | g Arg  | Arg  | Leu | Gln | Gln | Val | Gly | Thr | Val | Ala | Lys | Leu |     |
|    | 45       |        |        | 50   |     |     |     |     | 55  |     |     |     |     | 60  |     |
|    | tgg atc  | tac co | g gtg  | aaa  | tcc | tgc | aaa | ggg | gtg | ccg | gtg | agc | gag | gct | 482 |
|    | Trp Ile  | Tyr Pi | o Val  | Lys  | Ser | Cys | Lys | Gly | Val | Pro | Val | Ser | Glu | Ala |     |
| 15 |          |        | 65     |      |     |     |     | 70  |     |     |     |     | 75  |     |     |
|    | gag tgc  | acg go | c atg  | ggg  | ctg | cgc | agc | ggc | aac | ctg | cgg | gac | agg | ttt | 530 |
|    | Glu Cys  | Thr A  | a Met  | Gly  | Leu | Arg | Ser | Gly | Asn | Leu | Arg | Asp | Arg | Phe |     |
|    |          |        | 30     |      |     |     | 85  |     |     |     |     | 90  |     |     |     |
|    | tgg ctg  | gtg a  | t aag  | gaa  | gat | gga | cac | atg | gtc | act | gcc | cga | cag | gag | 578 |
| 20 | Trp Leu  | Val I  | le Lys | Glu  | Asp | Gly | His | Met | Val | Thr | Ala | Arg | Gln | Glu |     |
|    |          | 95     |        |      |     | 100 |     |     |     |     | 105 |     |     |     |     |
|    | cct cgc  | ctc g  | tg cto | ato  | tcc | atc | att | tat | gag | aat | aac | tgc | ctg | atc | 626 |
|    | Pro Arg  | Leu V  | al Leu | ılle | Ser | Ile | Ile | Tyr | Glu | Așn | Asn | Cys | Leu | Ile |     |
|    | 110      |        |        |      | 115 |     |     |     |     | 120 | )   |     |     |     |     |
| 25 | ttc agg  | gct c  | ca gad | ato  | gac | cag | ctg | gtt | ttg | cct | ago | aag | cag | cct | 674 |

|    | Phe | Arg | Ala | Pro | Asp   | Met   | Asp   | Gln  | Leu   | Val   | Leu   | Pro   | Ser | Lys   | Gln   | Pro |      |
|----|-----|-----|-----|-----|-------|-------|-------|------|-------|-------|-------|-------|-----|-------|-------|-----|------|
|    | 125 |     |     |     |       | 130   |       |      |       |       | 135   |       |     |       |       | 140 |      |
|    | tcc | tca | aac | aaa | ctc   | cac   | aac   | tgc  | agg   | ata   | ttt   | ggc   | ctt | gac   | att   | aaa | 722  |
|    | Ser | Ser | Asn | Lys | Leu   | His   | Asn   | Cys  | Arg   | Ile   | Phe   | Gly   | Leu | Asp   | Ile   | Lys |      |
| 5  |     |     |     |     | 145   |       |       |      |       | 150   |       |       |     |       | 155   |     |      |
|    | ggc | aga | gac | tgt | ggc   | aat   | gag   | gca  | gct   | aag   | tgg   | ttc   | acc | aac   | ttc   | ttg | 770  |
|    | Gly | Arg | Asp | Cys | Gly   | Asn   | Glu   | Ala  | Ala   | Lys   | Trp   | Phe   | Thr | Asn   | Phe   | Leu |      |
|    |     |     |     | 160 |       |       |       |      | 165   |       |       |       |     | 170   |       |     |      |
|    | aaa | act | gaa | gcg | tat   | aga   | ttg   | gtt  | caa   | ttt   | gag   | aca   | aac | atg   | aag   | gga | 818  |
| 10 | Lys | Thr | Glu | Ala | Tyr   | Arg   | Leu   | Val  | Gln   | Phe   | Glu   | Thr   | Asn | Met   | Lys   | Gly |      |
|    |     |     | 175 |     |       |       |       | 180  |       |       |       | •     | 185 |       |       | •   |      |
|    | aga | aca | tca | aga | aaa   | ctt   | ctc   | ccc  | act   | ctt   | gat   | cag   | aat | ttc   | cag   | gtg | 866  |
|    | Arg | Thr | Ser | Arg | Lys   | Leu   | Leu   | Pro  | Thr   | Leu   | Asp   | Gln   | Asn | Phe   | Gln   | Val |      |
|    |     | 190 |     |     |       |       | 195   |      |       |       |       | 200   |     |       |       | •   |      |
| 15 | gcc | tac | cca | gac | tac   | tgc   | ccg   | ctc  | ctg   | atc   | atg   | aca   | gat | gcc   | tcc   | ctg | 914  |
|    | Ala | Tyr | Pro | Asp | Tyr   | Суѕ   | Pro   | Leu  | Leu   | Ile   | Met   | Thr   | Asp | Ala   | Ser   | Leu |      |
|    | 205 |     |     |     |       | 210   | •     |      |       |       | 215   |       |     |       |       | 220 |      |
|    | gta | gat | ttg | aat | acc   | agg   | atg   | gag  | aag   | aaa   | atg   | aaa   | atg | gag   | aat   | ttc | 962  |
|    | Val | Asp | Leu | Asn | Thr   | Arg   | Met   | Glu  | Lys   | Lys   | Met   | Lys   | Met | Glu   | Asn   | Phe |      |
| 20 |     |     |     |     | 225   |       |       |      |       | 230   |       |       |     |       | 235   |     |      |
|    |     |     |     |     |       |       |       |      |       |       |       |       |     |       |       | acc | 1010 |
|    | Arg | Pro | Asn | Ile | · Val | . Val | Thr   | Gly  | Cys   | Asp   | Ala   | Phe   | Glu |       |       | Thr |      |
|    |     |     |     | 240 |       |       |       |      | 245   |       |       |       |     | 250   |       |     |      |
|    |     |     | gaa |     |       |       |       |      |       |       |       |       |     |       |       |     | 1058 |
| 25 | Trp | Asp | Glu | Lev | ı Lev | ı Ile | e Gly | ser, | : Val | . Glu | . Val | . Lys | Lys | : Val | . Met | Ala |      |

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|    |      |       | 255   |       |       |       |      | 260   |       |       |      |       | 265   |       |       |       |      |
|----|------|-------|-------|-------|-------|-------|------|-------|-------|-------|------|-------|-------|-------|-------|-------|------|
|    | tgc  | CCC   | agg   | tgt   | att   | ttg   | aca  | acg   | gtg   | gac   | cca  | gac   | act   | gga   | gtc   | ata   | 1106 |
|    | Cys  | Pro   | Arg   | Cys   | Ile   | Leu   | Thr  | Thr   | Val   | Asp   | Pro  | Asp   | Thr   | Gly   | Val   | Ile   |      |
|    |      | 270   |       |       |       |       | 275  |       |       |       |      | 280   |       |       |       |       |      |
| 5  | gac  | agg   | aaa   | cag   | cca   | ctg   | gac  | acc   | ctg   | aag   | agc  | tac   | cgc   | ctg   | tgt   | gat   | 1154 |
|    | Asp  | Arg   | Lys   | Gln   |       | Leu   | Asp  | Thr   | Leu   | Lys   | Ser  | Tyr   | Arg   | Leu   | Cys   | Asp   |      |
|    | 285  |       |       |       | c     | 290.  |      |       |       |       | 295  |       |       |       |       | 300   |      |
|    | cct  | tct   | gag   | agg   | gaa   | ttg   | tac  | aag   | ttg   | tct   | cca  | ctt   | ttt   | ggg   | atc   | tat   | 1202 |
| ~  | Pro  | Ser   | Glu   | Arg   | Glu   | Leu   | Tyr  | Lys   | Leu   | Ser   | Pro  | Leu   | Phe   | Gly   | Ile   | Tyr   |      |
| 10 |      |       |       |       | 305   |       |      |       |       | 310   |      |       |       |       | 315   |       |      |
|    | tat  | tca   | gtg   | gaa   | aaa   | att   | gga  | agc   | ctg   | aga   | gtt  | ggt   | gac   | cct   | gtg   | tat   | 1250 |
|    | Tyr  | Ser   | Val   | Glu   | Lys   | Ile   | Gly  | Ser   | Leu   | Arg   | Val  | Gly   | Asp   | Pro   | Val   | Tyr   |      |
|    |      |       |       | 320   |       |       |      |       | 325   |       |      |       |       | 330   |       |       |      |
|    | cgg  | atg   | gtg   | tagt  | gato  | gag t | gato | gato  | cc ac | tago  | gtga | a tat | ggct  | tca   |       |       | 1299 |
| 15 | Arg  | Met   | Val   |       |       |       |      |       |       |       |      |       |       |       |       |       |      |
|    |      |       | 335   |       |       |       |      |       |       |       |      |       |       |       |       |       |      |
|    | gcaa | accag | gga ç | ggat  | tgad  | et ga | gato | ettaa | a caa | cago  | agc  | aacq  | gatac | cat o | cagca | aatcc | 1359 |
|    | ttat | tato  | ca g  | gcctt | caac  | ct at | cttt | acco  | tgc   | jaaaa | ıcaa | tcto  | gatt  | tt 1  | tgact | tttca | 1419 |
|    | aagt | tgtg  | gta t | gcto  | ccago | jt ta | atgo | aagg  | j aaa | igtat | tag  | aggg  | ggga  | aat a | atgaa | agtat | 1479 |
| 20 | atat | cataa | at t  | ttag  | ggtac | et ga | aggo | ttta  | a aaa | ataa  | atta | agat  | cato  | caa a | aaato | ctatt | 1539 |
|    | ttga | atgt  | ta t  | cato  | ggcta | it ta | cact | ttta  | ctt   | ccto  | act  | ttaa  | tatt  | ga 1  | cgaat | aaagc | 1599 |
|    | aagt | ttaa  | atg a | aatca | act   |       |      |       |       |       |      |       |       |       |       |       | 1617 |
|    |      |       |       |       |       |       |      |       |       |       |      |       |       |       |       |       |      |

<210> 52

25 <211> 1749

|     | <21                | 2> D | NA   |      |       |       |      |      |      |       |       |       |      |       |       |        |     |
|-----|--------------------|------|------|------|-------|-------|------|------|------|-------|-------|-------|------|-------|-------|--------|-----|
|     | <213> Homo sapiens |      |      |      |       |       |      |      |      |       |       |       |      |       |       |        |     |
|     | <22                | 0>   |      |      |       |       |      |      |      |       |       |       |      |       |       |        |     |
|     | <22                | 1> C | DS   |      |       |       |      |      |      |       |       |       |      |       |       |        |     |
| 5   | <22                | 2> ( | 159) | (7   | 85)   |       |      |      |      |       |       |       |      |       |       |        |     |
|     | <40                | 0> 5 | 2    |      |       |       |      |      |      |       |       |       |      |       |       |        |     |
|     | gca                | cttc | cgg  | tggg | gagai | tt c  | cggc | ctgg | a gc | tccc  | aggg  | ccg   | agca | gac ( | cttg  | ggacct | 60  |
|     | gtg                | agcg | ctg  | catc | caati | ta a  | ccat | ggga | a gg | gtca  | gcac  | cag   | ccac | cag ( | ccc   | ttaggt | 120 |
|     | gag                | gact | ctc  | cctg | gggct | tc to | gctg | atgg | t tc | cgaat | tc at | tg ga | ag c | tg c  | gc go | cg gca | 176 |
| 10  |                    |      |      |      |       |       |      |      |      |       | Me    | et G  | lu L | eu A  | rg A  | la Ala |     |
|     |                    |      |      |      |       |       |      |      |      |       |       | 1     |      |       |       | 5      |     |
|     | ctg                | gtc  | ctg  | gtg  | gtc   | ctc   | ctc  | atc  | gcc  | ggg   | ggt   | ctc   | ttc  | atg   | ttc   | acc    | 224 |
|     | Leu                | Val  | Leu  | Val  | Val   | Leu   | Leu  | Ile  | Ala  | Gly   | Gly   | Leu   | Phe  | Met   | Phe   | Thr    |     |
|     |                    |      |      | 10   |       |       |      |      | 15   |       |       |       |      | 20    |       |        |     |
| 15  | tac                | aag  | tcc  | aca  | cag   | ttc   | aac  | gtg  | gag  | ggc   | ttc   | gcc   | ttg  | gtg   | ctg   | ggg    | 272 |
|     | Tyr                | Lys  | Ser  | Thr  | Gln   | Phe   | Asn  | Val  | Glu  | Gly   | Phe   | Ala   | Leu  | Val   | Leu   | Gly    |     |
|     |                    |      | 25   |      |       |       |      | 30   |      |       |       |       | 35   |       |       |        |     |
|     | gcc                | tcg  | ttc  | atc  | ggt   | ggc   | att  | cgc  | tgg  | acc   | ctc   | acc   | cag  | atg   | ctc   | ctg    | 320 |
|     | Ala                | Ser  | Phe  | Ile  | Gly   | Gly   | Ile  | Arg  | Trp  | Thr   | Leu   | Thr   | Gln  | Met   | Leu   | Leu    |     |
| 20  |                    | 40   |      |      |       |       | 45   |      |      |       |       | 50    |      |       |       |        |     |
|     | cag                | aag  | gct  | gaa  | ctc   | ggc   | ctc  | cag  | aat  | ccc   | atc   | gac   | acc  | atg   | ttc   | cac    | 368 |
|     |                    | Lys  | Ala  | Glu  | Leu   | Gly   | Leu  | Gln  | Asn  | Pro   | Ile   | Asp   | Thr  | Met   | Phe   | His    |     |
|     | 55                 |      |      |      |       | 60    |      |      |      |       | 65    |       |      |       |       | 70     |     |
| 0.5 |                    |      |      |      | atg   |       |      |      |      |       |       |       |      |       |       |        | 416 |
| 25  | Leu                | Gln  | Pro  | Leu  | Met   | Phe   | Leu  | Gly  | Leu  | Phe   | Pro   | Leu   | Phe  | Ala   | Val   | Phe    |     |

|    |     |     |     |     | 75  |     |     |          |     | 80  |     |      |     |      | 85   |       |     |
|----|-----|-----|-----|-----|-----|-----|-----|----------|-----|-----|-----|------|-----|------|------|-------|-----|
|    | gaa | ggt | ctc | cat | ttg | tcc | aca | tct      | gag | aaa | atc | ttc  | cgt | ttc  | cag  | gac   | 464 |
|    | Glu | Gly | Leu | His | Leu | Ser | Thr | Ser      | Glu | Lys | Ile | Phe  | Arg | Phe  | Gln  | Asp   |     |
|    |     |     |     | 90  |     |     |     |          | 95  |     |     |      |     | 100  |      |       |     |
| 5  | aca | ggg | ctg | ctc | ctg | cgg | gta | ctt      | ggg | agc | ctc | ttc  | ctt | ggc  | ggg  | att   | 512 |
|    | Thr | Gly | Leu | Leu | Leu | Arg | Val | Leu      | Gly | Ser | Leu | Phe  | Leu | Gly  | Gly  | Ile   |     |
|    |     |     | 105 |     |     |     |     | 110      |     |     |     |      | 115 |      | ,    |       |     |
|    | ctc | gcc | ttt | ggt | ttg | ggc | ttc | tct      | gag | ttc | ctc | ctg  | gtc | tcc  | aga  | acc   | 560 |
|    | Leu | Ala | Phe | Gly | Leu | Gly | Phe | Ser      | Glu | Phe | Leu | Leu  | Val | Ser  | Arg  | Thr   |     |
| LO |     | 120 |     |     |     |     | 125 |          |     |     |     | 130  |     |      |      |       |     |
|    | tcc | agc | ctc | act | ctc | tcc | att | gcc      | ggc | att | ttt | aag  | gaa | gtc  | tgc  | act   | 608 |
|    | Ser | Ser | Leu | Thr | Leu | Ser | Ile | Ala      | Gly | Ile | Phe | Lys  | Glu | Val  | Cys  | Thr   |     |
|    | 135 |     |     |     |     | 140 |     |          |     |     | 145 |      |     |      |      | 150 . |     |
|    | ttg | ctg | ttg | gca | gct | cat | ctg | ctg      | ggc | gat | cag | atc  | agc | ctc  | ctg  | aac   | 656 |
| 15 | Leu | Leu | Leu | Ala | Ala | His | Leu | Leu      | Gly | Asp | Gln | Ile  | Ser | Leu  | Leu  | Asn   |     |
|    | •   |     |     |     | 155 |     |     |          |     | 160 |     |      |     |      | 165  |       |     |
|    | tgg | ctg | ggc | ttc | gcc | ctc | tgc | ctc      | tcg | gga | ata | tcc  | ctc | cac  | gtt  | gcc   | 704 |
|    | Trp | Leu | Gly | Phe | Ala | Leu | Cys | Leu      | Ser | Gly | Ile | Ser  | Leu | His  | Val  | Ala   |     |
|    |     |     |     | 170 |     |     |     |          | 175 |     |     |      |     | 180  |      |       |     |
| 20 | ctc | aaa | gcc | ctg | cat | tcc | aga | ggt      | aac | cca | gag | tcc  | ctt | cca  | gaa  | gcc   | 752 |
|    | Leu | Lys | Ala | Leu | His | Ser | Arg | Gly      | Asn | Pro | Glu | Ser  | Leu | Pro  | Glu  | Ala   |     |
|    |     |     | 185 |     |     |     |     | 190      |     |     |     |      | 195 |      |      |       |     |
|    | tct | gtt | ttc | tgt | tct | tct | ccc | tgt      | gac | tct | tag | tgat | tct | gatg | cagg | aa    | 802 |
|    | Ser | Val | Phe | Cys | Ser | Ser | Pro | Cys<br>, | Asp | Ser |     |      |     |      |      |       |     |
| 25 |     | 200 |     |     |     |     | 205 |          |     |     |     |      |     |      |      |       |     |

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|    | gtgtgcccgg | tggctctgct | gccgtcactc | ctctaggaag | atgtgggggt | catctccaga | 862  |
|----|------------|------------|------------|------------|------------|------------|------|
|    | gtgggtgggt | ggggcctggg | tgactcagca | cacatgcaaa | tcagagcaaa | ccaagaaaac | 922  |
|    | cacgactggg | cctgtaactg | tggtctctct | ctatcccaag | gtgatggtgg | ccccaaggcc | 982  |
|    | ttgaaggggc | tgggctccag | ccccgacctg | gagctgctgc | tccggagcag | ccagcgggag | 1042 |
| 5  | gaaggtgaca | atgaggagga | ggagtacttt | gtggcccagg | ggcagcagtg | accagccagg | 1102 |
|    | gcaaatggct | tagaagcagg | ccactcccca | gcctgctgcc | agcactcact | gtgctcaagc | 1162 |
|    | cgccagggct | catcatggta | gctgggagct | gtggacggga | gtcaccaggt | ggtggggcca | 1222 |
|    | agccagggac | tcatgacttt | tgcccctccc | ttcagagcct | ggtcacacaa | ggggcgagca | 1282 |
|    | ccaggccagc | ctgggactgg | ccagagctgg | gcccaagctg | cgctggaatc | gcagcaggag | 1342 |
| 10 | aggggagtgg | gctggttctt | cccaccactt | cccaggctct | gacagccgag | actcatttcc | 1402 |
|    | aaggcacagc | agctttctaa | agggactgag | tttggactgg | gttttggacc | tccaggggct | 1462 |
|    | ggagcttcat | cacctgggca | gtgtcttttc | tcagagagca | ggtttcttta | tagtttggaa | 1522 |
|    | ataaatġgtt | cacggtccac | tggccgcctt | gtgttgctgg | agacgtgggg | gcagggaggg | 1582 |
|    | gacagtgtgg | gcctggcctc | tcctttcctt | tccctgcctg | gagccttctt | caaatgtctg | 1642 |
| 15 | gtcttaagcc | aggcctcctt | cattttctcg | ctcctgttag | aacaccagtc | ccctccccag | 1702 |
|    | tggggcccca | ctgcacctgc | tggcaggaaa | taaatgaatg | tttactg    |            | 1749 |

· (p

<210> 53

<211> 1402

20 <212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (60)..(1280)

25 <400> 53

|    | tgc | cccc | agc ( | gcca | ggcg | cg g | gctg | cgct | c gg | tggc | ggcg | gcg | gggc | cct | cagg | cggcc | 59  |
|----|-----|------|-------|------|------|------|------|------|------|------|------|-----|------|-----|------|-------|-----|
|    | atg | gcg  | gca   | ggc  | gcc  | ggg  | gcc  | ggg  | tcc  | gcg  | ccg  | cgc | tgg  | ctg | agg  | gcg   | 107 |
|    | Met | Ala  | Ala   | Gly  | Ala  | Gly  | Ala  | Gly  | Ser  | Ala  | Pro  | Arg | Trp  | Leu | Arg  | Ala   |     |
|    | 1   |      |       |      | 5    |      |      |      |      | 10   |      |     |      |     | 15   |       |     |
| 5  | ctg | agc  | gag   | ccg  | ctg  | agc  | gcg  | gcg  | cag  | ctg  | cgg  | cga | ctg  | gag | gag  | cac   | 155 |
|    | Leu | Ser  | Glu   | Pro  | Leu  | Ser  | Ala  | Ala  | Gln  | Leu  | Arg  | Arg | Leu  | Glu | Glu  | His   |     |
|    |     |      |       | 20   |      |      |      |      | 25   |      |      |     |      | 30  |      |       |     |
|    | cgc | tac  | agc   | gcg  | gcg  | ggc  | gtc  | tcg  | ctg  | ctc  | gag  | ccg | ccg  | ctg | cag  | ctc   | 203 |
|    | Arg | Tyr  | Ser   | Ala  | Ala  | Gly  | Val  | Ser  | Leu  | Leu  | Glu  | Pro | Pro  | Leu | Gln  | Leu   |     |
| 10 |     |      | 35    |      |      |      |      | 40   |      |      |      |     | 45   |     |      |       |     |
|    | tac | tgg  | acc   | tgg  | ctg  | ctc  | cag  | tgg  | atc  | ccg  | ctc  | tgg | atg  | gcc | ccc  | aac   | 251 |
|    | Tyr | Trp  | Thr   | Trp  | Leu  | Leu  | Gln  | Trp  | Ile  | Pro  | Leu  | Trp | Met  | Ala | Pro  | Asn   |     |
|    |     | 50   |       |      |      |      | 55   |      |      |      |      | 60  |      |     |      |       |     |
|    | tcc | atc  | acc   | ctg  | ctg  | ggg  | ctc  | gcc  | gtc  | aac  | gtg  | gtc | acc  | acg | ctc  | gtg   | 299 |
| 15 | Ser | Ile  | Thr   | Leu  | Leu  | Gly  | Leu  | Ala  | Val  | Asn  | Val  | Val | Thr  | Thr | Leu  | Val   |     |
|    | 65  |      |       |      |      | 70   |      |      |      |      | 75   |     |      |     |      | 80    |     |
|    | ctc | atc  | tcc   | tac  | tgt  | ccc  | acg  | gcc  | acc  | gaa  | gag  | gca | cca  | tac | tgg  | aca   | 347 |
|    | Leu | Ile  | Ser   | Tyr  | Cys  | Pro  | Thr  | Ala  | Thr  | Glu  | Glu  | Ala | Pro  | Tyr | Trp  | Thr   |     |
|    |     |      |       |      | 85   |      |      |      | •    | 90   |      |     |      | •   | 95   |       |     |
| 20 | tac | ctt  | tta   | tgt  | gca  | ctg  | gga  | ctt  | ttt  | att  | tac  | cag | tca  | ctg | gat  | gct   | 395 |
|    | Tyr | Leu  | Leu   | Cys  | Ala  | Leu  | Gly  | Leu  | Phe  | Ile  | Tyr  | Gln | Ser  | Leu | Asp  | Ala   |     |
|    |     |      |       | 100  |      |      |      |      | 105  |      |      |     |      | 110 |      |       |     |
|    | att | gat  | ggg   | aaa  | caa  | gcc  | aga  | aga  | aca  | aac  | tct  | tgt | tcc  | cct | tta  | ggg   | 443 |
|    | Ile | Asp  | Gly   | Lys  | Gln  | Ala  | Arg  | Arg  | Thr  | Asn  | Ser  | Cys | Ser  | Pro | Leu  | Gly   |     |
| 25 |     |      | 115   |      |      |      |      | 120  |      |      |      |     | 125  |     |      |       |     |

|    | gag | ctc | ttt | gac | cat | ggc | tgt | gac | tct | ctt | tcc | aca | gta | ttt | atg | gca | 491         |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------------|
|    | Glu | Leu | Phe | Asp | His | Gly | Cys | Asp | Ser | Leu | Ser | Thr | Val | Phe | Met | Ala |             |
|    |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |             |
|    | gtg | gga | gct | tca | att | gcc | gct | cgc | tta | gga | act | tat | cct | gac | tgg | ttt | 539         |
| 5  | Val | Gly | Ala | Ser | Ile | Ala | Ala | Arg | Leu | Gly | Thr | Tyr | Pro | Asp | Trp | Phe |             |
|    | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |             |
|    | ttt | ttc | tgc | tct | ttt | att | ggg | atg | ttt | gtg | ttt | tat | tgc | gct | cat | tgg | 587         |
|    | Phe | Phe | Cys | Ser | Phe | Ile | Gly | Met | Phe | Val | Phe | Tyr | Cys | Ala | His | Trp |             |
|    |     |     |     |     | 165 |     |     |     | *   | 170 |     |     |     |     | 175 |     |             |
| 10 | cag | act | tat | gtt | tca | ggc | atg | ttg | aga | ttt | gga | aaa | gtg | gat | gta | act | 635         |
|    | Gln | Thr | Tyr | Val | Ser | Gly | Met | Leu | Arg | Phe | Gly | Lys | Val | Asp | Val | Thr |             |
|    |     |     |     | 180 |     |     |     |     | 185 |     |     | ·;  |     | 190 |     |     |             |
|    | gaa | att | cag | ata | gct | tta | gtg | att | gtc | ttt | gtg | ttg | tct | gca | ttt | gga | 683         |
|    | Glu | Ile | Gln | Ile | Ala | Leu | Val | Ile | Val | Phe | Val | Leu | Ser | Ala | Phe | Gly |             |
| 15 |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |             |
|    | gga | gca | aca | atg | tgg | gac | tat | acg | att | cct | att | cta | gaa | ata | aaa | ttg | <b>7</b> 31 |
|    | Gly | Ala | Thr | Met | Trp | Asp | Tyr | Thr | Ile | Pro | Ile | Leu | Glu | Ile | Lys | Leu |             |
|    |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |             |
|    | aag | atc | ctt | сса | gtt | ctt | gga | ttt | cta | ggt | gga | gta | ata | ttt | tcc | tgt | 779         |
| 20 | Lys | Ile | Leu | Pro | Val | Leu | Gly | Phe | Leu | Gly | Gly | Val | Ile | Phe | Ser | Cys |             |
|    | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |             |
|    | tca | aat | tat | ttc | cat | gtt | atc | ctc | cat | ggt | ggt | gtt | ggc | aag | aat | gga | 827         |
|    | Ser | Asn | Tyr | Phe | His | Val | Ile | Leu | His | Gly | Gly | Val | Gly | Lys | Asn | Gly |             |
|    |     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |             |
| 25 | tcc | act | ata | gca | ggc | acc | agt | gtc | ttg | tca | cct | gga | ctc | cac | ata | gga | 875         |

|    | Ser | Thr | Ile | Ala   | Gly   | Thr   | Ser | Val | Leu   | Ser   | Pro | Gly   | Leu   | His   | Ile | Gly |      |
|----|-----|-----|-----|-------|-------|-------|-----|-----|-------|-------|-----|-------|-------|-------|-----|-----|------|
|    |     |     |     | 260   |       |       |     |     | 265   |       |     |       |       | 270   |     |     |      |
|    | cta | att | att | ata   | ctg   | gca   | ata | atg | atc   | tat   | aaa | aag   | tca   | gca   | act | gat | 923  |
|    | Leu | Ile | Ile | Ile   | Leu   | Ala   | Ile | Met | Ile   | Tyr   | Lys | Lys   | Ser   | Ala   | Thr | Asp |      |
| 5  |     |     | 275 |       |       |       |     | 280 |       |       |     |       | 285   |       |     |     |      |
|    | gtg | ttt | gaa | aag   | cat   | cct   | tgt | ctt | tat   | atc   | cta | atg   | ttt   | gga   | tgt | gtc | 971  |
|    | Val | Phe | Glu | Lys   | His   | Pro   | Cys | Leu | Tyr   | Ile   | Leu | Met   | Phe   | Gly   | Cys | Val |      |
|    |     | 290 |     |       |       |       | 295 |     |       |       |     | 300   |       |       |     |     |      |
|    | ttt | gct | aaa | gtc   | tca   | caa   | aaa | tta | gtg   | gta   | gct | cac   | atg   | acc   | aaa | agt | 1019 |
| 10 | Phe | Ala | Lys | Val   | Ser   | Gln   | Lys | Leu | Val   | Val   | Ala | His   | Met   | Thr   | Lys | Ser |      |
|    | 305 |     |     |       |       | 310   |     |     |       |       | 315 |       |       |       |     | 320 |      |
|    | gaa | cta | tat | ctt   | caa   | gac   | act | gtc | ttt   | ttg   | ggg | cca   | ggt   | ctt   | ttg | ttt | 1067 |
|    | Glu | Leu | Tyr | Leu   | Gln   | Asp   | Thr | Val | Phe   | Leu   | Gly | Pro   | Gly   | Leu   | Leu | Phe |      |
|    |     |     |     |       | 325   |       |     |     |       | 330   |     |       |       |       | 335 |     |      |
| 15 | tta | gac | cag | tac   | ttt   | aat   | aac | ttt | ata   | gac   | gaa | tat   | gtt   | gtt   | cta | tgg | 1115 |
|    | Leu | Asp | Gln | Tyr   | Phe   | Asn   | Asn | Phe | Ile   | Asp   | Glu | Tyr   | Val   | Val   | Leu | Trp |      |
|    |     |     |     | 340   |       |       |     |     | 345   |       |     |       |       | 350   |     |     |      |
|    | atg | gca | atg | gtg   | att   | tct   | tca | ttt | gat   | atg   | gtg | ata   | tac   | ttt   | agt | gct | 1163 |
|    | Met | Ala | Met | . Val | Ile   | Ser   | Ser | Phe | Asp   | Met   | Val | . Ile | Tyr   | Phe   | Ser | Ala |      |
| 20 |     |     | 355 | •     |       |       |     | 360 |       |       |     |       | 365   | 1     |     |     |      |
|    | ttg | tgc | ctg | caa   | att   | . tca | aga | cac | ctt   | cat   | cta | aat   | ata   | ttc   | aag | act | 1211 |
|    | Leu | Cys | Leu | ı Gln | Ile   | Ser   | Arg | His | Leu   | His   | Let | ı Asn | Ile   | Phe   | Lys | Thr |      |
|    |     | 370 | )   |       |       |       | 375 |     |       |       |     | 380   | )     |       |     |     |      |
|    | gca | tgt | cat | caa   | gca   | cct   | gaa | cag | gtt   | caa   | gtt | ctt   | tct   | tca   | aag | agt | 1259 |
| 25 | Ala | Cys | His | Glr   | n Ala | Pro   | Glu | Gln | . Val | . Glm | va. | Let   | ı Sei | : Ser | Lys | Ser |      |

114/346

385 390 395 400

cat cag aat aac atg gat tgaagagact tccgaacact tgctatctct 1307 His Gln Asn Asn Met Asp

405

5 tgctgctgct gtttcatgga aggagatatt aaacatttgt ttaattttta tttaagtgtt 1367 atacctattt cagcaaataa aatatttcat tgctt 1402

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gccaatacca ccaccagatt cttcttgaa gtcaactttt gagatcttca ctaagtacac 180
gttggtgtct gaagattcac acgagtgcct ctggtaatca ttttcttcag ggaatcacag 240
tctctcctct cagcaaagca tccactgtac tgaactttgc ttttggaaac atcttctcc 300
tgagacctcg ttgaaagaaa ctctctggtg tcatactttc caat atg gag gtg aag 356
Met Glu Val Lys

1

aac ttt gca gtt tgg gat tat gtt gta ttt gca gcc ctc ttt ttc att 404

25 Asn Phe Ala Val Trp Asp Tyr Val Val Phe Ala Ala Leu Phe Phe Ile

|    | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |     |     |     | 20  |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | tcc | tct | gga | att | ggg | gtg | ttc | ttt | gcc | att | aag | gag | aga | aaa | aag | gca | 452 |
|    | Ser | Ser | Gly | Ile | Gly | Val | Phe | Phe | Ala | Ile | Lys | Glu | Arg | Lys | Lys | Ala |     |
|    |     | •   |     |     | 25  |     |     |     |     | 30  |     |     |     |     | 35  |     |     |
| 5  | act | tcc | cga | gag | ttc | ctg | gtt | ggg | gga | agg | caa | atg | agc | ttt | ggc | cct | 500 |
|    | Thr | Ser | Arg | Glu | Phe | Leu | Val | Gly | Gly | Arg | Gln | Met | Ser | Phe | Gly | Pro |     |
|    |     |     |     | 40  |     |     |     |     | 45  |     |     |     |     | 50  |     |     |     |
|    | gtc | ggc | ttg | tct | ctg | aca | gcc | agc | ttc | atg | tca | gct | gtc | acg | gtc | ctg | 548 |
|    | Val | Gly | Leu | Ser | Leu | Thr | Ala | Ser | Phe | Met | Ser | Ala | Val | Thr | Val | Leu |     |
| 10 |     |     | 55  |     |     |     |     | 60  |     |     |     |     | 65  |     |     |     |     |
|    | ggg | acc | cct | tct | gaa | gtc | tac | cgc | ttt | ggg | gca | tcc | ttc | cta | gtc | ttc | 596 |
|    | Gly | Thr | Pro | Ser | Glu | Val | Tyr | Arg | Phe | Gly | Ala | Ser | Phe | Leu | Val | Phe |     |
|    |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |     |     |     |     |     |
|    | ttc | att | gct | tac | cta | ttt | gtc | atc | ctc | tta | aca | tca | gag | ctc | ttt | ctc | 644 |
| 15 | Phe | Ile | Ala | Tyr | Leu | Phe | Val | Ile | Leu | Leu | Thr | Ser | Glu | Leu | Phe | Leu |     |
|    | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |     |     |     | 100 |     |
|    | cct | gtg | ttc | tac | aga | tct | ggt | atc | acc | agc | act | tat | gag | tac | tta | caa | 692 |
|    | Pro | Val | Phe | Tyr | Arg | Ser | Gly | Ile | Thr | Ser | Thr | Tyr | Glu | Tyr | Leu | Gln |     |
|    |     |     |     |     | 105 |     |     |     |     | 110 |     |     |     |     | 115 |     |     |
| 20 | cta | cga | ttc | aac | aaa | cca | gtt | cgc | tat | gct | gcc | aca | gtc | atc | tac | att | 740 |
|    | Leu | Arg | Phe | Asn | Lys | Pro | Val | Arg | Tyr | Ala | Ala | Thr | Val | Ile | Tyr | Ile |     |
|    |     |     |     | 120 |     |     |     |     | 125 |     |     |     |     | 130 |     |     |     |
|    | gta | cag | acg | att | ctc | tac | aca | gga | gtg | gtg | gtg | tat | gct | cct | gcc | ctg | 788 |
|    | Val | Gln | Thr | Ile | Leu | Tyr | Thr | Gly | ۷al | Val | Val | Tyr | Ala | Pro | Ala | Leu |     |
| 25 |     |     | 135 |     |     |     |     | 140 |     |     |     |     | 145 |     |     |     |     |

|    | gca | ctc | aat | caa | gtg | act | ggg | ttt | gat | ctc | tgg | ggc | tct | gtg | ttt | gca | 836  |   |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|---|
|    | Ala | Leu | Asn | Gln | Val | Thr | Gly | Phe | Asp | Leu | Trp | Gly | Ser | Val | Phe | Ala |      |   |
|    |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |     |     |     |     |      |   |
|    | aca | gga | att | gtt | tgc | aca | ttc | tac | tgt | acc | ctg | gga | gga | tta | aaa | gca | 884  |   |
| 5  | Thr | Gly | Ile | Val | Cys | Thr | Phe | Tyr | Cys | Thr | Leu | Gly | Gly | Leu | Lys | Ala |      |   |
|    | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |     |     |     | 180 |      |   |
|    | gtg | gtg | tgg | aca | gat | gca | ttt | cag | atg | gtt | gtc | atg | att | gtg | ggc | ttc | 932  |   |
|    | Val | Val | Trp | Thr | Asp | Ala | Phe | Gln | Met | Val | Val | Met | Ile | Val | Gly | Phe |      |   |
|    |     |     |     |     | 185 |     |     |     |     | 190 | •   |     |     |     | 195 |     |      |   |
| 10 | tta | acg | gtt | ctc | att | caa | gga | tca | act | cat | gct | ggg | gga | ttc | cac | aat | 980  | 3 |
|    | Leu | Thr | Val | Leu | Ile | Gln | Gly | Ser | Thr | His | Ala | Gly | Gly | Phe | His | Asn |      | 4 |
|    |     |     |     | 200 |     |     |     |     | 205 |     |     |     |     | 210 |     |     |      |   |
|    | gta | tta | gag | caa | tca | aca | aat | gga | tct | cga | cta | cat | ata | ttt | gac | ttt | 1028 |   |
|    | Val | Leu | Glu | Gln | Ser | Thr | Asn | Gly | Ser | Arg | Leu | His | Ile | Phe | Asp | Phe |      |   |
| 15 |     |     | 215 |     |     |     |     | 220 |     |     |     | •   | 225 |     |     |     |      |   |
|    | gat | gta | gat | cct | ctc | agg | cga | cac | act | ttt | tgg | act | atc | aca | gtg | gga | 1076 |   |
|    | Asp | Val | Asp | Pro | Leu | Arg | Arg | His | Thr | Phe | Trp | Thr | Ile | Thr | Val | Gly |      |   |
|    |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |     |     |     |     |      |   |
|    | gga | act | ttt | act | tgg | ctc | gga | atc | tat | ggg | gtc | aat | caa | tca | act | att | 1124 |   |
| 20 | Gly | Thr | Phe | Thr | Trp | Leu | Gly | Ile | Tyr | Gly | Val | Asn | Gln | Ser | Thr | Ile |      |   |
|    | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |     |     |     | 260 |      |   |
|    | cag | cga | tgc | atc | tct | tgc | aaa | aca | gaa | aag | cat | gct | aag | ctt | gcc | ttg | 1172 |   |
|    | Gln | Arg | Cys | Ile | Ser | Cys | Lys | Thr | Glu | Lys | His | Ala | Lys | Leu | Ala | Leu |      |   |
|    |     |     |     |     | 265 |     |     |     |     | 270 |     |     |     |     | 275 |     |      |   |
| 25 | tat | ttt | aac | ttg | ctg | ggt | ctc | tgg | atc | att | ctg | gtg | tgt | gct | gtc | ttc | 1220 |   |

|    | Tyr | Phe | Asn | Leu | Leu | Gly | Leu | Trp | Ile | Ile | Leu | Val | Cys | Ala | Val | Phe |      |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|    |     |     |     | 280 |     |     |     |     | 285 |     |     |     |     | 290 |     |     |      |
|    | tct | ggc | tta | atc | atg | tac | tct | cac | ttt | aaa | gac | tgt | gac | cct | tgg | act | 1268 |
|    | Ser | Gly | Leu | Ile | Met | Tyr | Ser | His | Phe | Lys | Asp | Cys | Asp | Pro | Trp | Thr |      |
| 5  |     |     | 295 |     |     |     |     | 300 |     |     |     |     | 305 |     |     |     |      |
|    | tct | ggc | atc | atc | tca | gca | cca | gac | cag | ctg | atg | ccg | tac | ttt | gtc | atg | 1316 |
|    | Ser | Gly | Ile | Ile | Ser | Ala | Pro | Asp | Gln | Leu | Met | Pro | Tyr | Phe | Val | Met |      |
|    |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |     |     |     | ٠   |      |
|    | gag | ata | ttt | gcc | aca | atg | cca | gga | ctg | cca | gga | ctt | ttt | gtg | gct | tgt | 1364 |
| 10 | Glu | Ile | Phe | Ala | Thr | Met | Pro | Gly | Leu | Pro | Gly | Leu | Phe | Val | Ala | Cys |      |
|    | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |     |     |     | 340 |      |
|    | gcc | ttc | agt | gga | act | ctg | agc | acc | gtg | gct | tcc | agc | atc | aat | gcc | ttg | 1412 |
|    | Ala | Phe | Ser | Gly | Thr | Leu | Ser | Thr | Val | Ala | Ser | Ser | Ile | Asn | Ala | Leu |      |
|    |     |     |     |     | 345 |     |     |     |     | 350 |     |     |     |     | 355 |     |      |
| 15 | gca | aca | gtg | acc | ttt | gag | gat | ttt | gtc | aag | agc | tgt | ttt | cct | cat | ctc | 1460 |
|    | Ala | Thr | Val | Thr | Phe | Glu | Asp | Phe | Val | Lys | Ser | Cys | Phe | Pro | His | Leu |      |
|    |     |     |     | 360 |     |     |     |     | 365 |     |     |     |     | 370 |     |     |      |
|    | tcc | gac | aag | ctg | agc | acc | tgg | atc | agt | aaa | ggc | tta | tgt | ctc | tta | ttt | 1508 |
|    | Ser | Asp | Lys | Leu | Ser | Thr | Trp | Ile | Ser | Lys | Gly | Leu | Cys | Leu | Leu | Phe |      |
| 20 |     |     | 375 |     |     |     |     | 380 |     |     |     |     | 385 |     |     |     |      |
|    | ggc | gtg | atg | tgt | acc | tct | atg | gct | gtg | gct | gca | tct | gtc | atg | gga | ggt | 1556 |
|    | Gly | Val | Met | Cys | Thr | Ser | Met | Ala | Val | Ala | Ala | Ser | Val | Met | Gly | Gly |      |
|    |     | 390 |     |     |     |     | 395 |     |     |     |     | 400 |     |     |     |     |      |
|    | gtt | gtg | cag | gct | tcc | ctc | agc | att | cac | ggc | atg | tgt | gga | gga | cca | atg | 1604 |
| 25 | Val | Val | Gln | Ala | Ser | Leu | Ser | Ile | His | Gly | Met | Cys | Gly | Gly | Pro | Met |      |

|    | 405 |     |     |     |     | 410 |          |     |     |     | 415 |     |     |     |     | 420 |      |
|----|-----|-----|-----|-----|-----|-----|----------|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|    | ctg | ggc | tta | ttc | tcc | ctg | gga      | atc | gtg | ttc | cct | ttt | gtg | aac | tgg | aag | 1652 |
|    | Leu | Gly | Leu | Phe | Ser | Leu | Gly      | Ile | Val | Phe | Pro | Phe | Val | Asn | Trp | Lys |      |
|    |     |     |     |     | 425 |     |          |     |     | 430 |     |     |     |     | 435 |     |      |
| 5  | ggt | gca | cta | gga | ggt | ctt | ctt      | act | gga | atc | acc | ttg | tca | ttt | tgg | gtg | 1700 |
|    | Gly | Ala | Leu | Gly | Gly | Leu | Leu      | Thr | Gly | Ile | Thr | Leu | Ser | Phe | Trp | Val |      |
|    |     |     |     | 440 |     |     |          |     | 445 |     |     |     |     | 450 |     |     |      |
|    | gcc | att | ggg | gcc | ttc | att | tac      | cct | gca | cca | gcc | tct | aag | aca | tgg | cct | 1748 |
|    | Ala | Ile | Gly | Ala | Phe | Ile | Tyr      | Pro | Ala | Pro | Ala | Ser | Lys | Thr | Trp | Pro |      |
| 10 |     |     | 455 |     |     |     |          | 460 |     |     |     |     | 465 |     |     |     |      |
|    | ttg | cct | cta | tca | aca | gac | caa      | tgt | atc | aaa | tca | aat | gtg | aca | gca | aca | 1796 |
|    | Leu | Pro | Leu | Ser | Thr | Asp | Gln      | Cys | Ile | Lys | Ser | Asn | Val | Thr | Ala | Thr |      |
|    |     | 470 |     |     |     |     | 475      |     |     |     |     | 480 |     |     |     |     |      |
|    | ggg | cct | cca | gta | cta | tcc | agc<br>· | aga | cct | gga | ata | gct | gat | acc | tgg | tac | 1844 |
| 15 | Gly | Pro | Pro | Val | Leu | Ser | Ser      | Arg | Pro | Gly | Ile | Ala | Asp | Thr | Trp | Tyr |      |
|    | 485 |     |     |     |     | 490 |          |     |     |     | 495 |     |     |     |     | 500 |      |
|    | tcg | atc | tcc | tac | ctt | tac | tac      | agt | gca | gtg | ggc | tgc | tta | gga | tgc | att | 1892 |
|    | Ser | Ile | Ser | Tyr | Leu | Tyr | Tyr      | Ser | Ala | Val | Gly | Cys | Leu | Gly | Cys | Ile |      |
|    |     |     |     |     | 505 |     |          |     |     | 510 |     |     |     |     | 515 |     |      |
| 20 | gtt | gct | gga | gta | atc | atc | agc      | ctc | ata | aca | ggt | cgc | caa | aga | ggt | gag | 1940 |
|    | Val | Ala | Gly | Val | Ile | Ile | Ser      | Leu | Ile | Thr | Gly | Arg | Gln | Arg | Gly | Glu |      |
|    |     |     |     | 520 |     |     |          |     | 525 |     |     |     |     | 530 |     |     |      |
|    |     |     |     |     |     |     |          | _   |     | _   |     |     |     |     |     | ttt | 1988 |
|    | Asp | Ile | Gln | Pro | Leu | Leu | Ile      |     | Pro | Val | Cys | Aşn |     | Phe | Cys | Phe |      |
| 25 |     |     | 535 |     |     |     |          | 540 |     |     |     |     | 545 |     |     |     |      |

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|    | tgg  | tct   | aag   | aag   | tac   | aaa   | aca   | cta   | tgc   | tgg   | tgc  | gga  | gtt               | cag   | cat               | gac    | 2036 |
|----|------|-------|-------|-------|-------|-------|-------|-------|-------|-------|------|------|-------------------|-------|-------------------|--------|------|
|    | Trp  | Ser   | Lys   | Lys   | Tyr   | Lys   | Thr   | Leu   | Cys   | Trp   | Cys  | Gly  | Val               | Gln   | His               | Asp    |      |
|    |      | 550   |       |       |       |       | 555   |       |       |       |      | 560  |                   |       |                   |        |      |
|    | agt  | ggg   | aca   | gag   | cag   | gaa   | aac   | ctt   | gag   | aat   | ggc  | agt  | gcc               | cgg   | aaa               | cag    | 2084 |
| 5  | Ser  | Gly   | Thr   | Glu   | Gln   | Glu   | Asn   | Leu   | Glu   | Asn   | Gly  | Ser  | Ala               | Arg   | Lys               | Gln    |      |
|    | 565  |       |       |       |       | 570   |       |       |       |       | 575  |      |                   |       |                   | 580    |      |
|    | ggg  | gct   | gaa   | tct   | gtc   | tta   | cag   | aac   | gga   | ctc   | aga  | aga  | gaa               | agc   | ctg               | gta    | 2132 |
|    | Gly  | Ala   | Glu   | Ser   | Val   | Leu   | Gln   | Asn   | Gly   | Leu   | Arg  | Arg  | Glu               | Ser   | Leu               | Val    |      |
|    |      | •     |       |       | 585   |       |       |       |       | 590   |      |      |                   |       | 595               |        |      |
| 10 | cat  | gtt   | cca   | ggc   | tat   | gat   | cct   | aag   | gac   | aaa   | agc  | tac  | aac               | aat   | atg               | gca    | 2180 |
|    | His  | ۷al   | Pro   | Gly   | Tyr   | Asp   | Pro   | Lys   | Asp   | Lys   | Ser  | Tyr  | Asn               | Asn   | Met               | Ala    |      |
|    |      |       |       | 600   |       |       |       |       | 605   |       |      |      |                   | 610   |                   |        |      |
|    | ttt  | gag   | act   | acc   | cat   | ttc   | taaq  | ggcaa | ata d | cctgt | atga | aa t | gcac              | acac  | a                 |        | 2228 |
|    | Phe  | Glu   | Thr   | Thr   | His   | Phe   |       |       |       |       |      |      |                   |       |                   |        |      |
| 15 |      |       | 615   |       |       |       |       |       |       |       |      |      |                   |       |                   |        |      |
|    | cac  | gtgca | aat a | acaca | acaca | ac ac | caca  | caaa  | e te  | cacat | cact | tcti | tgcci             | tac 1 | ttgti             | tagtag | 2288 |
|    | atat | tgtat | tag t | ttgc  | catto | gc ta | agaaq | gaca  | g gga | atgto | ctgg | tgc  | ctati             | ttc 1 | tact              | tattta | 2348 |
|    | taad | ctaca | atg ( | caaa  | atgad | ct gi | tctc  | tcgg  | g ata | attc  | tttg | aaa  | gact              | cca a | actt <sup>.</sup> | tcacag | 2408 |
|    | agaa | aaago | cca a | acct  | gctc  | ca aa | atgc  | cctt  | g act | tacti | tcct | tct  | tgaa <sup>.</sup> | taa i | atta              | gggctg | 2468 |
| 20 | gati | ttc   |       |       |       |       |       |       |       |       |      |      |                   |       |                   |        | 2474 |
|    |      |       |       |       |       |       |       |       |       |       |      |      |                   |       |                   |        |      |
|    | <210 | 0> 5  | 5     |       |       |       |       |       |       |       |      |      |                   |       |                   |        |      |
|    | <21  | 1> 32 | 296   |       |       |       |       |       |       |       |      |      |                   |       |                   |        |      |
|    | <212 | 2> Di | NA.   |       |       |       |       |       |       |       |      |      |                   |       |                   |        |      |
|    |      |       |       |       |       |       |       |       |       |       |      |      |                   |       |                   |        |      |

25 <213> Homo sapiens

# 120/346

|    | <220 | >     |       |       |       |       |       |       |       |      |      |      |      |       |       |        |     |
|----|------|-------|-------|-------|-------|-------|-------|-------|-------|------|------|------|------|-------|-------|--------|-----|
|    | <221 | .> CE | os    |       |       |       |       |       |       |      |      |      |      |       |       |        |     |
|    | <222 | !> (1 | .42). | . (76 | 58)   |       |       |       |       |      |      |      |      |       |       |        |     |
|    | <400 | > 55  | 5     |       |       |       |       |       |       |      |      |      |      |       |       |        |     |
| 5  | ttcg | ıgggg | ggc a | agco  | gege  | gg ag | gggga | aaacg | g tgo | gegg | jccg | aagg | ggaa | igc g | ggago | ccggcg | 60  |
|    | ccgç | ctgo  | cgc a | ıgagç | gaged | cg ct | ctc   | geege | c cgc | caco | ctcg | gcto | ggaç | icc o | cacga | aggctg | 120 |
|    | ccgc | atco  | ctg c | ccto  | ggaa  | ac a  | atg   | gga   | ctc   | ggc  | gcg  | cga  | ggt  | gct   | tgg   | gcc    | 171 |
|    |      |       |       |       |       |       | Met   | Gly   | Leu   | Gly  | Ala  | Arg  | Gly  | Ala   | Trp   | Ala    |     |
|    |      |       |       |       |       |       | 1     |       |       |      | 5    |      |      |       |       | 10     |     |
| 10 | gcg  | ctg   | ctc   | ctg   | ggg   | acg   | ctg   | cag   | gtg   | cta  | gcg  | ctg  | ctg  | ggg   | gcc   | gcc    | 219 |
|    | Ala  | Leu   | Leu   | Leu   | Gly   | Thr   | Leu   | Gln   | Val   | Leu  | Ala  | Leu  | Leu  | Gly   | Ala   | Ala    |     |
|    |      |       |       |       | 15    |       |       |       |       | 20   |      |      |      |       | 25    |        |     |
|    | cat  | gaa   | agc   | gca   | gcc   | atg   | gcg   | gca   | tct   | gca  | aac  | ata  | gag  | aat   | tct   | ggg    | 26  |
|    | His  | Glu   | Ser   | Ala   | Ala   | Met   | Ala   | Ala   | Ser   | Ala  | Asn  | Ile  | Glu  | Asn   | Ser   | Gly    |     |
| 15 |      | •     |       | 30    |       |       |       |       | 35    |      |      |      |      | 40    |       |        |     |
|    | ctt  | cca   | cac   | aac   | tcc   | agt   | gct   | aac   | tca   | aca  | gag  | act  | ctc  | caa   | cat   | gtg    | 315 |
|    | Leu  | Pro   | His   | Asn   | Ser   | Ser   | Ala   | Asn   | Ser   | Thr  | Glu  | Thr  | Leu  | Gln   | His   | Val    |     |
|    |      |       | 45    |       |       |       |       | 50    |       |      |      |      | 55   |       |       |        |     |
|    | cct  | tct   | gac   | cat   | aca   | aat   | gaa   | act   | tcc   | aac  | agt  | act  | gtg  | aaa   | cca   | cca    | 363 |
| 20 | Pro  | Ser   | Asp   | His   | Thr   | Asn   | Glu   | Thr   | Ser   | Asn  | Ser  | Thr  | Val  | Lys   | Pro   | Pro    |     |
|    |      | 60    |       |       |       |       | 65    |       |       |      |      | 70   |      |       |       |        |     |
|    | act  | tca   | gtt   | gcc   | tca   | gac   | tcc   | agt   | aat   | aca  | acg  | gtc  | acc  | acc   | atg   | aaa    | 41  |
|    | Thr  | Ser   | Val   | Ala   | Ser   | Asp   | Ser   | Ser   | Asn   | Thr  | Thr  | Val  | Thr  | Thr   | Met   | Lys    |     |
|    | 75   |       |       |       |       | 80    |       |       |       |      | 85   |      |      |       |       | 90     |     |

cct aca gcg gca tct aat aca aca aca cca ggg atg gtc tca aca aat 459

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|    | Pro  | Thr   | Ala   | Ala   | Ser   | Asn   | Thr   | Thr   | Thr              | Pro  | Gly  | Met  | Val   | Ser   | Thr   | Asn    |     |
|----|------|-------|-------|-------|-------|-------|-------|-------|------------------|------|------|------|-------|-------|-------|--------|-----|
|    |      |       |       |       | 95    |       |       |       |                  | 100  |      |      |       |       | 105   |        |     |
|    | atg  | act   | tct   | acc   | acc   | tta   | aag   | tct   | aca <sup>.</sup> | ccc  | aaa  | aca  | aca   | agt   | gtt   | tca    | 507 |
|    | Met  | Thr   | Ser   | Thr   | Thr   | Leu   | Lys   | Ser   | Thr              | Pro  | Lys  | Thr  | Thr   | Ser   | Val   | Ser    |     |
| 5  |      |       |       | 110   |       |       |       |       | 115              |      |      |      |       | 120   |       |        |     |
|    | cag  | aac   | aca   | tct   | cag   | ata   | tca   | aca   | tcc              | aca  | atg  | acc  | gta   | acc   | cac   | aat    | 555 |
|    | Gln  | Asn   | Thr   | Ser   | Gln   | Ile   | Ser   | Thr   | Ser              | Thr  | Met  | Thr  | Val   | Thr   | His   | Asn    |     |
|    |      |       | 125   |       |       |       |       | 130   |                  |      |      |      | 135   |       |       |        |     |
|    | agt  | tca   | gtg   | aca   | tct   | gct   | gct   | tca   | tca              | gta  | aca  | atc  | aca   | aca   | act   | atg    | 603 |
| 10 | Ser  | Ser   | Val   | Thr   | Ser   | Ala   | Ala   | Ser   | Ser              | Val  | Thr  | Ile  | Thr   | Thr   | Thr   | Met    |     |
|    |      | 140   |       |       |       |       | 145   |       |                  |      |      | 150  |       |       |       |        |     |
|    | cat  | tct   | gaa   | gca   | aag   | aaa   | gga   | tca   | aaa              | ttt  | gat  | act  | ggg   | agc   | ttt   | gtt    | 651 |
|    | His  | Ser   | Glu   | Ala   | Lys   | Lys   | Gly   | Ser   | Lys              | Phe  | Asp  | Thr  | Gly   | Ser   | Phe   | Val    |     |
|    | 155  |       |       |       |       | 160   |       |       |                  |      | 165  |      |       |       |       | 170    |     |
| 15 | ggt  | ggt   | att   | gta   | tta   | acg   | ctg   | gga   | gtt              | tta  | tct  | att  | ctt   | tac   | att   | gga    | 699 |
|    | Gly  | Gly   | Ile   | Val   | Leu   | Thr   | Leu   | Gly   | Val              | Leu  | Ser  | Ile  | Leu   | Tyr   | Ile   | Gly    |     |
|    |      |       |       |       | 175   |       |       |       |                  | 180  |      |      |       |       | 185   |        |     |
|    | tgc  | aaa   | atg   | tat   | tac   | tca   | aga   | aga   | ggc              | att  | cgg  | tat  | cga   | acc   | ata   | gat    | 747 |
|    | Cys  | Lys   | Met   | Tyr   | Tyr   | Ser   | Arg   | Arg   | Gly              | Ile  | Arg  | Tyr  | Arg   | Thr   | Ile   | Asp    |     |
| 20 |      |       |       | 190   |       |       |       |       | 195              |      |      |      |       | 200   |       |        |     |
|    | gaa  | cat   | gat   | gcc   | atc   | att   | taaq  | ggaaa | atc o            | catg | gacc | aa g | gatg  | gaat  | ā     |        | 795 |
|    | Glu  | His   | Asp   | Ala   | Ile   | Ile   |       |       |                  |      |      |      |       |       |       |        |     |
|    |      |       | 205   |       |       |       |       |       |                  |      |      |      |       |       |       |        |     |
|    | caga | attga | atg ( | ctgc  | cctai | cc aa | atta  | attti | t gg1            | ttai | ttaa | tag  | ttta  | aaa ( | caata | attctc | 855 |
| 25 | ttt  | ttgaa | aaa 1 | tagta | ataaa | ac a  | ggcca | atgc  | a tai            | taat | gtac | agt  | gtati | tac ( | gtaaa | atatgt | 915 |

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aaagattett caaggtaaca agggtttggg ttttgaaata aacatetgga tettatagae 975 cgttcataca atggttttag caagttcata gtaagacaaa caagtcctat ctttttttt 1035 ggctggggtg ggggcattgg tcacatatga ccagtaattg aaagacgtca tcactgaaag 1095 acagaatgcc atctgggcat acaaataaga agtttgtcac agcactcagg attttgggta 1155 tettttgtag etcacataaa gaactteagt getttteaga getggatata tettaattae 1215 taatgccaca cagaaattat acaatcaaac tagatctgaa gcataattta agaaaaacat 1275 caacattttt tgtgctttaa actgtagtag ttggtctaga aacaaaatac tccaagaaaa 1335 agaaaatttt caaataaaac ccaaaataat agctttgctt agccctgtta gggatccatt 1395 ggagcattaa ggagcacata tttttattaa cttcttttga qctttcaatq ttqatqtaat 1455 ttttgttctc tgtgtaattt aggtaaactg cagtgtttaa cataataatg ttttaaagac 1515 ttagttgtca gtattaaata atcctggcat tatagggaaa aaacctccta gaaqttagat 1575 tatttgctac tgtgagaata ttgtcaccac tggaagttac tttagttcat ttaattttaa 1635 ttttatattt tgtgaatatt ttaagaactg tagagctgct ttcaatatct agaaattttt 1695 aattgagtgt aaacacacct aactttaaga aaaagaaccg cttgtatgat tttcaaaaga 1755 acatttagaa ttctatagag tcaaaactat agcgtaatgc tgtgtttatt aagccaggga 1815 ttgtgggact tcccccaggc aactaaacct gcaggatgaa aatgctatat tttctttcat 1875 gcactgtcga tattactcag atttggggaa atgacatttt tatactaaaa caaacaccaa 1935 aatattttag aataaattct tagaaagttt tgagaggaat ttttagagag gacatttcct 1995 cettectgat ttggatatte ceteaaatee eteetettae teeatgetga aggagaagta 2055 ctctcagatg cattatgtta atggagagaa aaagcacagt attgtagaga caccaatatt 2115 agctaatgta ttttggagtg ttttccattt tacagtttat attccagcac tcaaaactca 2175 gggtcaagtt ttaacaaaag aggtatgtag tcacagtaaa tactaagatg gcatttctat 2235 ctcagagggc caaagtgaat cacaccagtt tctgaaggtc ctaaaaatag ctcagatgtc 2295 ctaatgaaca tgcacctaca tttaatagga gtacaataaa actgttgtca gcttttgttt 2355 tacagagaac gctagatatt aagaattttq aaatqqatca tttctacttq ctqtqcattt 2415

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taaccaataa totgatgaat atagaaaaaa atgatccaaa atatggatat gattggatgt 2475 atgtaacaca tacatggagt atggaggaaa ttttctgaaa aatacattta gattaqttta 2535 gtttgaagga gaggtgggct gatggctgag ttgtatgtta ctaacttqqc cctqactqqt 2595 tgtgcaacca ttgcttcatt tctttgcaaa atgtagttaa gatatacttt attctaatga 2655 5 aggiorttta aattigtooa otgoattott ggtatttoac tacttoaagt cagtoagaac 2715 ttcgtagacc gacctgaagt ttctttttga atacttgttt ctttagcact ttgaagatag 2775 aaaaaccact ttttaagtac taagtcatca tttgccttga aagtttcctc tgcattgggt 2835 ttgaagtagt ttagttatgt ctttttctct gtatgtaagt agtataattt gttactttca 2895 aatacccgta ctttgaatgt aggttttttt gttgttgtta tctataaaaa ttgagggaaa 2955 10 tggttatgca aaaaaatatt ttgctttgga ccatatttct taagcataaa aaaaatgctc 3015 agttttgctt gcattccttg agaatgtatt tatctgaaga tcaaaacaaa caatccagat 3075 gtataagtac taggcagaag ccaattttaa aattteettq aataateeat qaaaggaata 3135 attcaaatac agataaacag agttggcagt atattatagt gataattttg tattttcaca 3195 aaaaaaaagt taaactcttc ttttcttttt attataatga ccagcttttg gtatttcatt 3255 15 gttaccaagt tctattttta gaataaaatt gttctccttc t 3296

<210> 56

<211> 1818

<212> DNA

20 <213> Homo sapiens

<220>

<221> CDS

<222> (26)..(1534)

<400> 56

25 aaaaaacccg cgcagtggcc cggcg atg tcg ctc gtg ctg cta agc ctg gcc

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|    |     |     |     |     |     |     |     | Met | Ser | Leu | Val | Leu | Leu | Ser | Leu | Ala |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    |     |     |     |     |     |     |     | 1   |     |     |     | 5   |     |     |     |     |     |
|    | gcg | ctg | tgc | agg | agc | gcc | gta | ccc | cga | gag | ccg | acc | gtt | caa | tgt | ggc | 100 |
|    | Ala | Leu | Cys | Arg | Ser | Ala | Val | Pro | Arg | Glu | Pro | Thr | Val | Gln | Cys | Gly | ٠.  |
| 5  | 10  |     |     |     |     | 15  |     |     |     |     | 20  |     |     |     |     | 25  |     |
|    | tct | gaa | act | ggg | cca | tct | cca | gag | tgg | atg | cta | caa | cat | gat | cta | atc | 148 |
|    | Ser | Glu | Thr | Gly | Pro | Ser | Pro | Glu | Trp | Met | Leu | Gln | His | Asp | Leu | Ile |     |
|    |     |     |     |     | 30  |     |     |     |     | 35  |     |     |     |     | 40  |     |     |
|    | ccg | gga | gac | ttg | agg | gac | ctc | cga | gta | gaa | cct | gtt | aca | act | agt | gtt | 196 |
| 10 | Pro | Gly | Asp | Leu | Arg | Asp | Leu | Arg | Val | Glu | Pro | Val | Thr | Thr | Ser | Val |     |
|    |     |     |     | 45  |     |     |     |     | 50  |     |     |     |     | 55  |     |     |     |
|    | gca | aca | ggg | gac | tat | tca | att | ttg | atg | aat | gta | agc | tgg | gta | ctc | cgg | 244 |
|    | Ala | Thr | Gly | Asp | Tyr | Ser | Ile | Leu | Met | Asn | Val | Ser | Trp | Val | Leu | Arg |     |
|    |     |     | 60  |     |     |     |     | 65  |     |     |     |     | 70  |     |     |     |     |
| 15 | gca | gat | gcc | agc | atc | cgc | ttg | ttg | aag | gcc | acc | aag | att | tgt | gtg | acg | 292 |
|    | Ala | Asp | Ala | Ser | Ile | Arg | Leu | Leu | Lys | Ala | Thr | Lys | Ile | Cys | Val | Thr |     |
|    |     | 75  |     |     |     |     | 80  |     |     |     |     | 85  |     |     |     |     |     |
|    | ggc | aaa | agc | aac | ttc | cag | tcc | tac | agc | tgt | gtg | agg | tgc | aat | tac | aca | 340 |
|    | Gly | Lys | Ser | Asn | Phe | Gln | Ser | Tyr | Ser | Cys | Val | Arg | Cys | Asn | Tyr | Thr |     |
| 20 | 90  |     |     |     |     | 95  |     |     |     |     | 100 |     |     |     |     | 105 |     |
|    | gag | gcc | ttc | cag | act | cag | acc | aga | ccc | tct | ggt | ggt | aaa | tgg | aca | ttt | 388 |
|    | Glu | Ala | Phe | Gln | Thr | Gln | Thr | Arg | Pro | Ser | Gly | Gly | Lys | Trp | Thr | Phe |     |
|    |     |     |     |     | 110 |     |     |     |     | 115 |     |     |     |     | 120 |     |     |
|    | tcc | tac | atc | ggc | ttc | cct | gta | gag | ctg | aac | aca | gtc | tat | ttc | att | ggg | 436 |

Ser Tyr Ile Gly Phe Pro Val Glu Leu Asn Thr Val Tyr Phe Ile Gly

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|    |     |     |     | 125 |     |     |     |     | 130 |     |     |     |     | 135 |     |     |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | gcc | cat | aat | att | cct | aat | gca | aat | atg | aat | gaa | gat | ggc | cct | tcc | atg | 484 |
|    | Ala | His | Asn | Ile | Pro | Asn | Ala | Asn | Met | Asn | Glu | Asp | Gly | Pro | Ser | Met |     |
|    |     |     | 140 |     |     |     |     | 145 |     |     |     |     | 150 |     |     |     |     |
| 5  | tct | gtg | aat | ttc | acc | tca | cca | ggc | tgc | cta | gac | cac | ata | atg | aaa | tat | 532 |
|    | Ser | Val | Asn | Phe | Thr | Ser | Pro | Gly | Cys | Leu | Asp | His | Ile | Met | Lys | Tyr |     |
|    |     | 155 |     |     |     |     | 160 |     |     |     |     | 165 |     |     |     |     |     |
|    | aaa | aaa | aag | tgt | gtc | aag | gcc | gga | agc | ctg | tgg | gat | ccg | aac | atc | act | 580 |
|    | Lys | Lys | Lys | Cys | Val | Lys | Ala | Gly | Ser | Leu | Trp | Asp | Pro | Asn | Ile | Thr |     |
| 10 | 170 |     |     |     |     | 175 |     |     |     |     | 180 |     |     |     |     | 185 |     |
|    | gct | tgt | aag | aag | aat | gag | gag | aca | gta | gaa | gtg | aac | ttc | aca | acc | act | 628 |
|    | Ala | Cys | Lys | Lys | Asn | Glu | Glu | Thr | Val | Glu | Val | Asn | Phe | Thr | Thr | Thr |     |
|    |     |     |     |     | 190 |     |     |     |     | 195 |     |     |     |     | 200 |     |     |
|    | ccc | ctg | gga | aac | aga | tac | atg | gct | ctt | atc | caa | cac | agc | act | atc | atc | 676 |
| 15 | Pro | Leu | Gly | Asn | Arg | Tyr | Met | Ala | Leu | Ile | Gln | His | Ser | Thr | Ile | Ile |     |
|    |     |     |     | 205 |     |     |     |     | 210 |     |     |     |     | 215 |     |     |     |
|    | ggg | ttt | tct | cag | gtg | ttt | gag | cca | cac | cag | aag | aaa | caa | acg | cga | gct | 724 |
|    | Gly | Phe | Ser | Gln | Val | Phe | Glu | Pro | His | Gln | Lys | Lys | Gln | Thr | Arg | Ala |     |
|    |     |     | 220 |     |     |     |     | 225 |     |     |     |     | 230 |     |     |     |     |
| 20 | tca | gtg | gtg | att | cca | gtg | act | ggg | gat | agt | gaa | ggt | gct | acg | gtg | cag | 772 |
|    | Ser | Val | Val | Ile | Pro | Val | Thr | Gly | Asp | Ser | Glu | Gly | Ala | Thr | Val | Gln |     |
|    |     | 235 |     |     |     | ,   | 240 |     |     |     |     | 245 |     |     |     |     |     |
|    | ctg | act | cca | tat | ttt | cct | act | tgt | ggc | agc | gac | tgc | atc | cga | cat | aaa | 820 |
|    | Leu | Thr | Pro | Tyr | Phe | Pro | Thr | Cys | Gly | Ser | Asp | Cys | Ile | Arg | His | Lys |     |
| 25 | 250 |     |     |     |     | 255 |     |     |     |     | 260 |     |     |     |     | 265 |     |

|    | gga | aca | gtt | gtg | ctc | tgc | cca | caa | aca | ggc | gtc | cct | ttc | cct | ctg | gat | 868  |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|    | Gly | Thr | Val | Val | Leu | Cys | Pro | Gln | Thr | Gly | Val | Pro | Phe | Pro | Leu | Asp |      |
|    |     |     |     |     | 270 |     |     |     |     | 275 |     |     |     |     | 280 |     |      |
|    | aac | aac | aaa | agc | aag | ccg | gga | ggc | tgg | ctg | cct | ctc | ctc | ctg | ctg | tct | 916  |
| 5  | Asn | Asn | Lys | Ser | Lys | Pro | Gly | Gly | Trp | Leu | Pro | Leu | Leu | Leu | Leu | Ser |      |
|    |     |     |     | 285 |     |     |     |     | 290 |     |     |     |     | 295 |     |     |      |
|    | ctg | ctg | gtg | gcc | aca | tgg | gtg | ctg | gtg | gca | ggg | atc | tat | cta | atg | tgg | 964  |
|    | Leu | Leu | Val | Ala | Thr | Trp | Val | Leu | Val | Ala | Gly | Ile | Tyr | Leu | Met | Trp |      |
|    |     |     | 300 |     |     |     |     | 305 |     |     |     |     | 310 |     |     |     |      |
| 10 | agg | cac | gaa | agg | atc | aag | aag | act | tcc | ttt | tct | acc | acc | aca | cta | ctg | 1012 |
|    | Arg | His | Glu | Arg | Ile | Lys | Lys | Thr | Ser | Phe | Ser | Thr | Thr | Thr | Leu | Leu |      |
|    |     | 315 |     |     |     |     | 320 |     |     |     |     | 325 |     |     |     |     |      |
|    | ccc | ccc | att | aag | gtt | ctt | gtg | gtt | tac | cca | tct | gaa | ata | tgt | ttc | cat | 1060 |
|    | Pro | Pro | Ile | Lys | Val | Leu | Val | Val | Tyr | Pro | Ser | Glu | Ile | Cys | Phe | His |      |
| 15 | 330 |     |     |     |     | 335 |     |     |     |     | 340 |     |     |     |     | 345 |      |
|    | cac | aca | att | tgt | tac | ttc | act | gaa | ttt | ctt | caa | aac | cat | tgc | aga | agt | 1108 |
|    | His | Thr | Ile | Cys | Tyr | Phe | Thr | Glu | Phe | Leu | Gln | Asn | His | Cys | Arg | Ser |      |
|    |     |     |     |     | 350 |     |     |     |     | 355 |     |     |     |     | 360 |     |      |
|    | gag | gtc | atc | ctt | gaa | aag | tgg | cag | aaa | aag | aaa | ata | gca | gag | atg | ggt | 1156 |
| 20 | Glu | Val | Ile | Leu | Glu | Lys | Trp | Gln | Lys | Lys | Lys | Ile | Ala | Glu | Met | Gly |      |
|    |     |     |     | 365 |     |     |     |     | 370 |     |     |     |     | 375 |     |     |      |
|    | cca | gtg | cag | tgg | ctt | gcc | act | caa | aag | aag | gca | gca | gac | aaa | gtc | gtc | 1204 |
|    | Pro | Val | Gln | Trp | Leu | Ala | Thr | Gln | Lys | Lys | Ala | Ala | Asp | Lys | Val | Val |      |
|    |     |     | 380 |     |     |     |     | 385 |     |     |     |     | 390 |     |     |     |      |
| 25 | ttc | ctt | ctt | tcc | aat | gac | gtc | aac | agt | gtg | tgc | gat | ggt | acc | tgt | ggc | 1252 |
|    |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |      |

|    | Phe  | Leu   | Leu   | Ser   | Asn   | Asp   | Val   | Asn   | Ser   | Val   | Cys | Asp  | Gly   | Thr   | Cys   | Gly    |      |
|----|------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-----|------|-------|-------|-------|--------|------|
|    |      | 395   |       |       |       |       | 400   |       |       |       |     | 405  |       |       |       |        |      |
|    | aag  | agc   | gag   | ggc   | agt   | ccc   | agt   | gag   | aac   | tct   | caa | gac  | ctc   | ttc   | ccc   | ctt    | 1300 |
|    | Lys  | Ser   | Glu   | Gly   | Ser   | Pro   | Ser   | Glu   | Asn   | Ser   | Gln | Asp  | Leu   | Phe   | Pro   | Leu    |      |
| 5  | 410  |       |       |       |       | 415   |       |       |       |       | 420 |      |       |       |       | 425    |      |
|    | gcc  | ttt   | aac   | ctt   | ttc   | tgc   | agt   | gat   | cta   | aga   | agc | cag  | att   | cat   | ctg   | cac    | 1348 |
|    | Ala  | Phe   | Asn   | Leu   | Phe   | Cys   | Ser   | Asp   | Leu   | Arg   | Ser | Gln  | Ile   | His   | Leu   | His    |      |
|    |      |       |       |       | 430   |       |       |       |       | 435   |     |      |       |       | 440   |        |      |
|    | aaa  | tac   | gtg   | gtg   | gtc   | tac   | ttt   | aga   | gag   | att   | gat | aca  | aaa   | gac   | gat   | tac    | 1396 |
| 10 | Lys  | Tyr   | Val   | Val   | Val   | Tyr   | Phe   | Arg   | Glu   | Ile   | Asp | Thr  | Lys   | Asp   | Asp   | Tyr    |      |
|    |      |       |       | 445   |       |       |       |       | 450   |       |     |      |       | 455   |       |        |      |
|    | aat  | gct   | ctc   | agt   | gtc   | tgc   | ccc   | aag   | tac   | cac   | ctc | atg  | aag   | gat   | gcc   | act    | 1444 |
|    | Asn  | Ala   | Leu   | Ser   | Val   | Суѕ   | Pro   | Lys   | Tyr   | His   | Leu | Met  | Lys   | Asp   | Ala   | Thr    |      |
|    |      |       | 460   |       |       |       |       | 465   |       |       |     |      | 470   |       |       |        |      |
| 15 | gct  | ttc   | tgt   | gca   | gaa   | ctt   | ctc   | cat   | gtc   | aag   | cag | cag  | gtg   | tca   | gca   | gga    | 1492 |
|    | Ala  | Phe   | Cys   | Ala   | Glu   | Leu   | Leu   | His   | Val   | Lys   | Gln | Gln  | Val   | Ser   | Ala   | Gly    |      |
|    |      | 475   |       |       |       |       | 480   |       |       |       |     | 485  |       |       |       |        |      |
|    | aaa  | aga   | tca   | caa   | gcc   | tgc   | cac   | gat   | ggc   | tgc   | tgc | tcc  | ttg   | tago  | ccad  | ccc    | 1541 |
|    | Lys  | Arg   | Ser   | Gln   | Ala   | Cys   | His   | Asp   | Gly   | Cys   | Cys | Ser  | Leu   |       |       |        |      |
| 20 | 490  |       |       |       |       | 495   |       |       |       |       | 500 |      |       |       |       |        |      |
|    | atga | agaag | gca a | agaga | acctt | a aa  | aggct | tcct  | ato   | ccad  | caa | ttad | cagg  | gaa a | aaaa  | gtgtg  | 1601 |
|    | atga | atcct | iga a | agctt | acta  | at go | cagco | ctaca | aac   | cagco | tta | gtaa | attaa | aaa d | catti | tatac  | 1661 |
|    | caat | caaaa | att t | tcaa  | aatat | t go  | ctaac | ctaat | gta   | agcat | taa | ctaa | acgat | tg q  | gaaad | ctacat | 1721 |
|    | ttad | caact | ctc a | aaago | ctgtt | t ta  | ataca | ataga | a aat | caat  | tac | agti | ttaa  | att 9 | gaaaa | ectata | 1781 |
| 25 | acca | attt  | ga t  | aato  | gcaad | a at  | aaaq  | gcato | : tto | agco  | :   |      |       |       |       |        | 1818 |

|    | <210 | > 57 |      |      |      |      |      |      |     |     |     |     |     |     |     |     |     |
|----|------|------|------|------|------|------|------|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | <211 | > 16 | 46   |      |      |      |      |      |     |     |     |     |     |     |     |     |     |
|    | <212 | > DN | A    |      |      |      |      |      |     |     |     |     |     |     |     |     |     |
| 5  | <213 | > Ho | mo s | apie | ens  |      |      |      |     |     |     |     |     |     |     |     |     |
|    | <220 | >    |      |      |      |      |      |      |     |     |     |     |     |     |     |     |     |
|    | <221 | > CD | S    |      |      |      |      |      |     |     |     |     |     |     |     |     |     |
|    | <222 | > (3 | 37)  | (104 | 17)  |      |      |      |     |     | •   |     |     |     |     |     |     |
|    | <400 | > 57 | ,    |      |      |      |      |      |     |     |     |     |     |     |     |     |     |
| LO | acgo | gago | tg d | ctgt | tttt | t to | ctgo | ttgg | acg | cgc | atg | agg | gcc | ccg | tcc | atg | 54  |
|    |      |      |      |      |      |      |      |      |     |     | Met | Arg | Ala | Pro | Ser | Met |     |
|    |      |      |      |      |      |      |      |      |     |     | 1   |     |     |     | 5   |     |     |
|    | gac  | cgc  | gcg  | gcc  | gtg  | gcg  | agg  | gtg  | ggc | gcg | gta | gcg | agc | gcc | agc | gtg | 102 |
|    | Asp  | Arg  | Ala  | Ala  | Val  | Ala  | Arg  | Val  | Gly | Ala | Val | Ala | Ser | Ala | Ser | Val |     |
| 15 |      |      |      | 10   |      |      |      |      | 15  |     |     |     |     | 20  |     |     |     |
| ·  | tgc  | gcc  | ctg  | gtg  | gcg  | ggg  | gtg  | gtg  | ctg | gct | cag | tac | ata | ttc | acc | ttg | 150 |
|    | Cys  | Ala  | Leu  | Val  | Ala  | Gly  | Val  | Val  | Leu | Ala | Gln | Tyr | Ile | Phe | Thr | Leu |     |
|    |      |      | 25   |      |      |      |      | 30   |     |     |     |     | 35  |     |     |     |     |
|    | aag  | agg  | aag  | acg  | ggg  | cgg  | aag  | acc  | aag | atc | atc | gag | atg | atg | cca | gaa | 198 |
| 20 | Lys  | Arg  | Lys  | Thr  | Gly  | Arg  | Lys  | Thr  | Lys | Ile | Ile | Glu | Met | Met | Pro | Glu |     |
|    |      | 40   |      |      |      |      | 45   |      |     |     |     | 50  |     |     |     |     |     |
|    | ttc  | cag  | aaa  | agt  | tca  | gtt  | cga  | atc  | aag | aac | cct | aca | aga | gta | gaa | gaa | 246 |
|    | Phe  | Gln  | Lys  | Ser  | Ser  | Val  | Arg  | Ile  | Lys | Asn | Pro | Thr | Arg | Val | Glu | Glu |     |
|    | 55   |      |      |      |      | 60   |      |      |     |     | 65  |     |     |     |     | 70  |     |
| 25 | a++  | atc  | tat  | aat  | ctt  | atc  | 222  | aaa  | aas | act | acc | 222 | ctt | сап | ata | ata | 294 |

|    | Ile | Ile | Суѕ | Gly | Leu | Ile | Lys | Gly | Gly | Ala | Ala | Lys | Leu | Gln | Ile | Ile |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    |     |     |     |     | 75  |     |     |     |     | 80  |     |     |     |     | 85  |     |     |
|    | acg | gac | ttt | gat | atg | aca | ctc | agt | aga | ttt | tca | tat | aaa | ggg | aaa | aga | 342 |
|    | Thr | Asp | Phe | Asp | Met | Thr | Leu | Ser | Arg | Phe | Ser | Tyr | Lys | Gly | Lys | Arg |     |
| 5  |     |     |     | 90  |     |     |     |     | 95  |     |     |     |     | 100 |     |     |     |
|    | tgc | cca | aca | tgt | cat | aat | atc | att | gac | aac | tgt | aag | ctg | gtt | aca | gat | 390 |
|    | Cys | Pro | Thr | Cys | His | Asn | Ile | Ile | Asp | Asn | Cys | Lys | Leu | Val | Thr | Asp |     |
|    |     | •   | 105 |     |     | •   |     | 110 |     |     |     |     | 115 |     |     |     |     |
|    | gaa | tgt | aga | aaa | aag | tta | ttg | caa | cta | aag | gaa | aaa | tat | tac | gct | att | 438 |
| 10 | Glu | Cys | Arg | Lys | Lys | Leu | Leu | Gln | Leu | Lys | Glu | Lys | Tyr | Tyr | Ala | Ile |     |
|    |     | 120 |     |     |     |     | 125 |     |     |     |     | 130 |     |     |     |     |     |
|    | gaa | gtt | gat | cct | gtt | ctt | act | gta | gaa | gag | aag | tac | cct | tat | atg | gtg | 486 |
|    | Glu | Val | Asp | Pro | Val | Leu | Thr | Val | Glu | Glu | Lys | Tyr | Pro | Tyr | Met | Val |     |
|    | 135 |     |     |     |     | 140 |     |     |     |     | 145 |     |     |     |     | 150 |     |
| 15 | gaa | tgg | tat | act | aaa | tca | cat | ggt | ttg | ctt | gtt | cag | caa | gct | tta | cca | 534 |
|    | Glu | Trp | Tyr | Thr | Lys | Ser | His | Gly | Leu | Leu | Val | Gln | Gln | Ala | Leu | Pro |     |
|    |     |     |     |     | 155 |     |     |     |     | 160 |     |     |     |     | 165 |     |     |
|    | aaa | gct | aaa | ctt | aaa | gaa | att | gtg | gca | gaa | tct | gac | gtt | atg | ctc | aaa | 582 |
|    | Lys | Ala | Lys | Leu | Lys | Glu | Ile | Val | Ala | Glu | Ser | Asp | Val | Met | Leu | Lys |     |
| 20 |     |     |     | 170 |     |     |     |     | 175 |     |     |     |     | 180 |     |     |     |
|    | gaa | gga | tat | gag | aat | ttc | ttt | gat | aag | ctc | caa | caa | cat | agc | atc | ccc | 630 |
|    | Glu | Gly | Tyr | Glu | Asn | Phe | Phe | Asp | Lys | Leu | Gln | Gln | His | Ser | Ile | Pro |     |
|    |     |     | 185 |     |     |     |     | 190 |     |     |     |     | 195 |     |     |     |     |
|    | gtg | ttc | ata | ttt | tcg | gct | gga | atc | ggc | gat | gta | cta | gag | gaa | gtt | att | 678 |
| 25 | Val | Phe | Ile | Phe | Ser | Ala | Gly | Ile | Gly | Asp | Val | Leu | Glu | Glu | Val | Ile |     |

|     | 200     |         |         | 205     |         | 210      |            |         |      |
|-----|---------|---------|---------|---------|---------|----------|------------|---------|------|
|     | cgt caa | gct ggt | gtt tat | cat ccc | aat gtc | aaa gtt  | gtg tcc    | aat ttt | 726  |
|     | Arg Gln | Ala Gly | Val Tyr | His Pro | Asn Val | Lys Val  | Val Ser    | Asn Phe |      |
|     | 215     |         | 220     |         |         | 225      |            | 230     |      |
| 5   | atg gat | ttt gat | gaa act | ggg gtg | ctc aaa | gga ttt  | aaa gga    | gaa cta | 774  |
|     | Met Asp | Phe Asp | Glu Thr | Gly Val | Leu Lys | Gly Phe  | Lys Gly    | Glu Leu |      |
|     |         |         | 235     |         | 240     |          | :          | 245     |      |
|     | att cat | gta ttt | aac aaa | cat gat | ggt gcc | ttg agg  | aat aca    | gaa tat | 822  |
|     | Ile His | Val Phe | Asn Lys | His Asp | Gly Ala | Leu Arg  | Asn Thr    | Glu Tyr |      |
| 10  | •       | 250     |         |         | 255     |          | 260        |         |      |
|     | ttc aat | caa cta | aaa gac | aat agt | aac ata | att ctt  | ctg gga g  | gac tcc | 870  |
|     | Phe Asn | Gln Leu | Lys Asp | Asn Ser | Asn Ile | Ile Leu  | Leu Gly I  | Asp Ser |      |
|     |         | 265     |         | 270     |         |          | 275        |         |      |
|     |         |         |         |         |         |          | gtt gag (  |         | 918  |
| 15  |         | Asp Leu | Arg Met |         | Gly Val | Ala Asn  | Val Glu I  | His Ile |      |
|     | 280     |         |         | 285     |         | 290      |            |         |      |
|     |         |         |         |         |         |          | ctt tta (  |         | 966  |
|     |         | Ile Gly |         | Asn Asp | Arg Val |          | Leu Leu (  | _       |      |
| 20  | 295     |         | 300     |         |         | 305      |            | 310     |      |
| 20  |         |         |         |         |         |          | gaa tca 1  |         | 1014 |
|     | Tyr Met | Asp Ser |         | Ile Val |         | Gln Asp  | Glu Ser    |         |      |
|     | ata     |         | 315     |         | 320     |          |            | 325     |      |
|     |         |         |         |         |         | taaacaag | rca ttctco | caaga   | 1064 |
| 25  | vat Ata |         | Ile Leu | сти гАЗ |         |          |            |         |      |
| 2,0 |         | 330     |         |         | 335     |          |            |         |      |

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agacetetet cetgtgggtg caattgaact gtteateegt teatettget gagagaetta 1124

tttataatat ateettaete tegaagtgtt eeetttgtat aactgaagta tttteagata 1184

tggtgaatge attgaetgga ageteetttt eteeacetet eteaacacae teeteacegt 1244

ateetttaac eeatttaaaa aaaaaaaaa getaaaatta gaaaaataae teeetaettt 1304

teeaaagtga attttgtagt ttaatgttat eatgeagett ttgaggagte ttttacactg 1364

ggaaagtttg tagaaatttt aaaataagtt ttatgaaatg gtgaaataat atgeatgatt 1424

ttaagtattg eeatttttgt aatttgggtt attatgetga tggtateace ateetetgaa 1484

attgtgttag gtttggttat tttgtetggg gaaaaaatat ttaetggaaa agactageag 1544 '

ttagtgttgg aaaaacetgg tggtgtttae aatgttgeta ateattacaa aacattetat 1604

attgaageae tgataataaa tatgaaatge aaaacetttt tt 1646

<210> 58

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<211> 1416

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<220>

<221> CDS

<222> (174)..(1196)

<400> 58

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gcttgcccc caccccggcc caggcaagcc accctgcccc cggccccac ctgcccgccc 120
cgcctgccct tcctcacccc ggtgcctgcg ggattgctgg agagaacgcg gcg atg 176
Met

1

25 gag ccg ggc agg acc cag ata aag ctt gac ccc agg tac aca gca gat 224

|    | Glu | Pro | Gly | Arg | Thr | Gln | Ile | Lys | Leu              | Asp | Pro | Arg | Tyr | Thr | Ala | Asp |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|------------------|-----|-----|-----|-----|-----|-----|-----|-----|
|    |     |     |     | 5   |     |     |     |     | 10               |     |     |     |     | 15  |     |     |     |
|    | ctt | ctg | gag | gtg | ctg | aag | acc | aat | tac              | ggc | atc | ccc | tcc | gcc | tgc | ttc | 272 |
|    | Leu | Leu | Glu | Val | Leu | Lys | Thr | Asn | Tyr              | Gly | Ile | Pro | Ser | Ala | Cys | Phe |     |
| 5  |     |     | 20  |     |     |     |     | 25  |                  |     |     |     | 30  |     |     |     |     |
|    | tct | cag | cct | ccc | aca | gca | gcc | caa | ctc              | ctg | aga | gcc | ctg | ggc | cct | gtg | 320 |
|    | Ser | Gln | Pro | Pro | Thr | Ala | Ala | Gln | Leu              | Leu | Arg | Ala | Leu | Gly | Pro | Val |     |
|    |     | 35  |     |     |     |     | 40  |     |                  |     |     | 45  |     |     |     |     |     |
|    | gaa | ctt | gcc | ctc | act | agc | atc | ctg | acc              | ttg | ctg | gcg | ctg | ggc | tcc | att | 368 |
| 10 | Glu | Leu | Ala | Leu | Thr | Ser | Ile | Leu | Thr              | Leu | Leu | Ala | Leu | Gly | Ser | Ile |     |
|    | 50  |     |     |     |     | 55  |     |     |                  |     | 60  |     |     |     |     | 65  |     |
|    | gcc | atc | ttc | ctg | gag | gat | gcc | gtc | tac              | ctg | tac | aag | aac | acc | ctt | tgc | 416 |
|    | Ala | Ile | Phe | Leu | Glu | Asp | Ala | Val | Tyr              | Leu | Tyr | Lys | Asn | Thr | Leu | Cys |     |
|    |     |     |     |     | 70  |     |     |     |                  | 75  |     |     |     |     | 80  |     |     |
| 15 | ccc | atc | aag | agg | cgg | act | ctg | ctc | tgg              | aag | agc | tcg | gca | ccc | acg | gtg | 464 |
|    | Pro | Ile | Lys | Arg | Arg | Thr | Leu | Leu | Trp              | Lys | Ser | Ser | Ala | Pro | Thr | Val |     |
|    |     |     |     | 85  |     |     |     |     | 90               |     |     |     |     | 95  |     |     |     |
|    | gtg | tct | gtg | ctg | tgc | tgc | ttt | ggt | ctc              | tgg | atc | cct | cgt | tcc | ctg | gtg | 512 |
|    | Val | Ser | Val | Leu | Cys | Cys | Phe | Gly | Leu              | Trp | Ile | Pro | Arg | Ser | Leu | Val |     |
| 20 |     |     | 100 |     |     |     |     | 105 |                  |     |     |     | 110 |     |     |     |     |
|    | ctg | gtg | gaa | atg | acc | atc | acc | tcg | ttt              | tat | gcc | gtg | tgc | ttt | tac | ctg | 560 |
|    | Leu | Val | Glu | Met | Thr | Ile | Thr | Ser | Phe              | Tyr | Ala | Val | Cys | Phe | Tyr | Leu |     |
|    |     | 115 |     |     |     |     | 120 |     |                  |     |     | 125 |     |     |     |     |     |
|    | ctg | atg | ctg | gtc | atg | gtg | gaa | ggc | ttt <sub>.</sub> | ggg | ggg | aag | gag | gca | gtg | ctg | 608 |
| 25 | Leu | Met | Leu | Val | Met | Val | Glu | Gly | Phe              | Glv | Gly | Lys | Glu | Ala | Val | Leu |     |

|    | 130 |     |     |     |     | 135 |             |     |     |     | 140 |     |     |     |     | 145 |     |
|----|-----|-----|-----|-----|-----|-----|-------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | agg | acg | ctg | agg | gac | acc | ccg         | atg | atg | gtc | cac | aca | ggc | ccc | tgc | tgc | 656 |
|    | Arg | Thr | Leu | Arg | Asp | Thr | Pro         | Met | Met | Val | His | Thr | Gly | Pro | Cys | Cys |     |
|    |     |     |     |     | 150 |     |             |     |     | 155 |     |     |     |     | 160 |     |     |
| 5  | tgc | tgc | tgc | ccc | tgc | tgt | cca         | cgg | ctg | ctg | ctc | acc | agg | aag | aag | ctt | 704 |
|    | Cys | Cys | Cys | Pro | Cys | Cys | Pro         | Arg | Leu | Leu | Leu | Thr | Arg | Lys | Lys | Leu |     |
|    |     |     |     | 165 |     |     |             |     | 170 |     |     |     |     | 175 |     |     |     |
|    | cag | ctg | ctg | atg | ttg | ggc | cct         | ttc | caa | tac | gcc | ttc | ttg | aag | ata | acg | 752 |
|    | Gln | Leu | Leu | Met | Leu | Gly | Pro         | Phe | Gln | Tyr | Ala | Phe | Leu | Lys | Ile | Thr |     |
| 10 |     |     | 180 |     |     |     |             | 185 |     |     |     |     | 190 |     |     |     |     |
|    | ctg | acc | ctg | gtg | ggc | ctg | ttt         | ctc | atc | ccc | gac | ggc | atc | tat | gac | cca | 800 |
|    | Leu | Thr | Leu | Val | Gly | Leu | Phe         | Leu | Ile | Pro | Asp | Gly | Ile | Tyr | Asp | Pro |     |
|    |     | 195 |     |     |     |     | 200         |     |     |     |     | 205 |     |     |     |     |     |
|    | gca | gac | att | tct | gag | ggg | agc         | aca | gct | cta | tgg | atc | aac | act | ttc | ctt | 848 |
| 15 | Ala | Asp | Ile | Ser | Glu | Gly | Ser         | Thr | Ala | Leu | Trp | Ile | Asn | Thr | Phe | Leu |     |
|    | 210 |     |     |     |     | 215 |             |     |     |     | 220 |     |     |     |     | 225 |     |
|    | ggc | gtg | tcc | aca | ctg | ctg | gct         | ctc | tgg | acc | ctg | ggc | atc | att | tcc | cgt | 896 |
|    | Gly | Val | Ser | Thr | Leu | Leu | Ala         | Leu | Trp | Thr | Leu | Gly | Ile | Ile | Ser | Arg |     |
|    |     |     |     |     | 230 |     |             |     |     | 235 |     |     |     |     | 240 |     |     |
| 20 | caa | gcc | agg | cta | cac | ctg | <b>g</b> gt | gag | cag | aac | atg | gga | gcc | aaa | ttt | gct | 944 |
|    | Gln | Ala | Arg | Leu | His | Leu | Gly         | Glu | Gln | Asn | Met | Gly | Ala | Lys | Phe | Ala |     |
| ,  |     |     |     | 245 |     |     |             |     | 250 |     |     |     |     | 255 |     |     |     |
|    | ctg | ttc | cag | gtt | ctc | ctc | atc         | ctg | act | gcc | cta | cag | ccc | tcc | atc | ttc | 992 |
|    | Leu | Phe | Gln | Val | Leu | Leu | Ile         | Leu | Thr | Ala | Leu | Gln | Pro | Ser | Ile | Phe |     |
| 25 |     |     | 260 |     |     |     |             | 265 |     |     |     |     | 270 |     |     |     |     |

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|    | tca gtc ttg gcc aac ggt ggg cag att gct tgt tcg cct ccc tat tcc     | 1040 |
|----|---|------|
|    | Ser Val Leu Ala Asn Gly Gly Gln Ile Ala Cys Ser Pro Pro Tyr Ser     |      |
|    | 275 280 285   |      |
|    | tct aaa acc agg tct caa gtg atg aat tgc cac ctc ctc ata ctg gag     | 1088 |
| 5  | Ser Lys Thr Arg Ser Gln Val Met Asn Cys His Leu Leu Ile Leu Glu     |      |
|    | 290 295 300 305   |      |
|    | act ttt cta atg act gtg ctg aca cga atg tac tac cga agg aaa gac     | 1136 |
|    | Thr Phe Leu Met Thr Val Leu Thr Arg Met Tyr Tyr Arg Arg Lys Asp     |      |
|    | 310 315 320   |      |
| 10 | cac aag gtt ggg tat gaa act ttc tct tct cca gac ctg gac ttg aac     | 1184 |
|    | His Lys Val Gly Tyr Glu Thr Phe Ser Ser Pro Asp Leu Asp Leu Asn     |      |
|    | 325 330 335   |      |
|    | ctc aaa gcc taaggtggat ggcttggaca atgaaaggat gctgtactca             | 1233 |
|    | Leu Lys Ala   |      |
| 15 | 340   |      |
|    | ttagaataca agatteettt aetgteeete aacettgace aaatgggaag catteeecet 1 | L293 |
|    | tgtcaacaca agctggcaga tacatttgac tctacagatg aaggtgaaca atgttagaat 1 | L353 |
|    | aaaattgctt tggatcttgc ctggaaggtg ttttaagttt tgtaataaac aagatgatgt 1 | L413 |
|    | ctg   | 1416 |
| 20 | •   |      |
|    | <210> 59  |      |
|    | <211> 1927  |      |
|    | <212> DNA   |      |
|    | <213> Homo sapiens  |      |
| 25 | <220>   |      |

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|    | <22. | I> CI | JS    |       |       |       |       |       |       |       |       |       |       |       |       |            |     |
|----|------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|------------|-----|
|    | <22  | 2> (8 | 39).  | . (76 | 0)    |       |       |       |       |       |       |       |       |       |       |            |     |
|    | <400 | O> 59 | 9     |       |       |       |       |       |       | •     |       |       |       |       |       |            |     |
|    | agct | tcca  | gtc ( | ctgg  | catct | tg co | ccga  | ggaga | a cca | acgct | tcct  | gga   | gctc  | tgc 1 | tgtc  | ttctca     | 60  |
| ·5 | ggga | agact | ct (  | gaggo | ctct  | gt to | gagaa | atc a | atg d | ctt 1 | tgg a | agg ( | cag ( | ctc a | atc 1 | tat        | 112 |
|    |      |       |       |       |       |       |       | ı     | let 1 | Leu : | Frp / | Arg ( | Gln 1 | Leu : | Ile : | fyr        |     |
|    |      |       |       |       |       |       |       |       | 1     |       |       |       | 5     |       |       |            |     |
|    | tgg  | caa   | ctg   | ctg   | gct   | ttg   | ttt   | ttc   | ctc   | cct   | ttt   | tgc   | ctg   | tgt   | caa   | gat        | 160 |
|    | Trp  | Gln   | Leu   | Leu   | Ala   | Leu   | Phe   | Phe   | Leu   | Pro   | Phe   | Cys   | Leu   | Cys   | Gln   | Asp        |     |
| 10 |      | 10    |       |       | •     |       | 15    |       | •     |       |       | 20    |       |       |       |            |     |
|    | gaa  | tac   | atg   | gag   | gtg   | agc   | gga   | aga   | act   | aat   | aaa   | gtg   | gtg   | gca   | aga   | ata        | 208 |
|    | Glu  | Tyr   | Met   | Glu   | Val   | Ser   | Gly   | Arg   | Thr   | Asn   | Lys   | Val   | Val   | Ala   | Arg   | Ile        |     |
|    | 25   |       |       |       |       | 30    |       |       |       |       | 35    |       |       |       | _     | 40         |     |
|    | gtg  | caa   | agc   | cac   | cag   | cag   | act   | ggc   | cgt   | agc   | ggc   | tcc   | agg   | agg   | gag   | aaa        | 256 |
| 15 |      |       |       | His   |       |       |       |       |       |       |       |       |       |       |       |            |     |
|    |      |       |       |       | 45    |       |       | -     | _     | 50    |       |       |       | _     | 55    | •          |     |
|    | gtg  | aga   | gag   | cgg   | agc   | cat   | cct   | aaa   | act   | aaa   | act   | ata   | σat   | aat   | aac   | act.       | 304 |
|    |      |       |       | Arg   |       |       |       |       |       |       |       |       |       |       |       |            |     |
|    |      | _     |       | 60    |       |       |       | •     | 65    | •     |       |       |       | 70    |       |            |     |
| 20 | tct  | aca   | gac   | cta   | aaa   | tcc   | cta   | aga   |       | gat   | gag   | cta   | cca   |       | CCC   | gag        | 352 |
|    |      |       |       | Leu   |       |       |       |       |       |       |       |       |       |       |       |            | 332 |
|    |      |       | 75    |       | -2-   |       |       | 80    |       |       |       |       | 85    |       |       | CIU        |     |
|    | αta  | nat   |       | cta   | acc   | can   | atc   |       | 202   | ++~   | taa   | 000   |       | tat   | 000   | <b>422</b> | 400 |
|    |      |       |       | Leu   |       |       |       |       |       |       |       |       |       |       |       |            | 400 |
| 25 | , u. | 90    | rup)  | ಎರಡ   | VT.0  | 111ج  | 95    | 1117. | TIIT. | FIIG  | ıτħ   | 100   | GTII  | SGI   | LTO   | GTII       |     |
|    |      | 20    |       |       |       |       | 20    |       |       |       |       | TUU   |       |       |       |            |     |

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|    | acc     | gga | gga | cta | ccc | cca | gac | tgc | agt  | aag | tgt | tgt  | cat  | gga  | gac  | tac        | 448 |
|----|---------|-----|-----|-----|-----|-----|-----|-----|------|-----|-----|------|------|------|------|------------|-----|
|    | Thr     | Gly | Gly | Leu | Pro | Pro | Asp | Cys | Ser  | Lys | Cys | Cys  | His  | Gly  | Asp  | Tyr        |     |
|    | 105     |     |     |     |     | 110 |     |     |      |     | 115 |      |      |      |      | 120        |     |
|    | agc     | ttt | cga | ggc | tac | caa | ggc | ccc | cct  | ggg | cca | ccg  | ggc  | cct  | cct  | ggc        | 496 |
| 5  | Ser     | Phe | Arg | Gly | Tyr | Gln | Gly | Pro | Pro  | Gly | Pro | Pro  | Gly  | Pro  | Pro  | Gly        |     |
|    |         |     |     |     | 125 |     |     |     |      | 130 |     |      |      |      | 135  |            |     |
|    | att     | cca | gga | aac | cat | gga | aac | aat | ggc  | aac | aat | gga  | gcc  | act  | ggt  | cat        | 544 |
|    | Ile     | Pro | Gly | Asn | His | Gly | Asn | Asn | Gly  | Asn | Asn | Gly  | Ala  | Thr  | Gly  | His        |     |
|    |         |     |     | 140 |     |     |     |     | 145  |     |     |      |      | 150  |      |            |     |
| 10 |         |     |     |     |     |     |     |     |      |     |     |      |      |      |      | cga        | 592 |
|    | Glu     | Gly | Ala | Lys | Gly | Glu | Lys |     | Asp  | Lys | Gly | Asp  |      | Gly  | Pro  | Arg        |     |
| •  |         |     | 155 |     |     |     |     | 160 |      |     |     |      | 165  |      |      |            |     |
|    |         |     |     |     |     |     |     |     |      |     |     |      |      |      |      | ggg        | 640 |
|    | Gly     |     | Arg | Gly | Gln | His | _   | Pro | Lys  | GIY | Glu |      |      | Tyr  | Pro  | Gly        |     |
| 15 | _ 1. 1. | 170 |     |     |     |     | 175 |     | ***  |     |     | 180  |      | ~~~  | 200  |            | 600 |
|    |         |     | Pro |     |     |     |     |     |      |     |     | •    |      |      |      | cac<br>Wie | 688 |
|    | 185     | PIO | PLO | GIU | Ten | 190 |     | мта | FILE | Mec | 195 |      | шеu  | Ala  | 1111 | 200        |     |
| •  |         | age | aat | cad | 220 |     |     | att | atc  | ttc |     |      | att  | nan  | acc  | aac        | 736 |
| 20 |         |     | Asn |     |     |     |     |     |      |     |     |      |      |      |      |            |     |
|    |         |     |     |     | 205 |     | 2   |     |      | 210 |     |      |      |      | 215  |            |     |
|    | att     | gga | aac | ttc |     |     | tca | tga | ctgg |     |     | gggg | cc c | cagt | atca | g          | 78  |
|    |         |     | Asn |     |     |     |     |     |      | _   |     |      |      |      |      |            |     |
|    |         | _   |     | 220 |     |     |     |     |      |     |     |      |      |      |      |            |     |
|    |         |     |     |     |     |     |     |     |      |     |     |      |      |      |      |            |     |

gtgtgtattt cttcaccttc agcatgatga agcatgagga tgttgaggaa gtgtatgtgt 847

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accttatgca caatggcaac acagtcttca gcatgtacag ctatgaaatg aagggcaaat 907 cagatacatc cagcaatcat gctgtgctga agctagccaa aggggatgag gtttggctgc 967 gaatgggcaa tggcgctctc catggggacc accaacgctt ctccaccttt gcaqqattcc 1027 tgctctttga aactaagtaa atatatgact agaatagctc cactttgggg aagacttgta 1087 gctgagctga tttgttacga tctgaggaac attaaagttg agggttttac attgctgtat 1147 tcaaaaaatt attggttgca atgttgttca cgctacaggt acaccaataa tgttggacaa 1207 ttcaggggct cagaagaatc aaccacaaaa tagtcttctc agatgacctt gactaatata 1267 ctcagcatct ttatcactct ttccttggca cctaaaagat aattctcctc tgacgcaggt 1327 tggaaatatt tttttctatc acagaagtca tttgcaaaga attttgacta ctctgctttt 1387 aatttaatac cagttttcag gaacccctga agttttaagt tcattattct ttataacatt 1447 tgagagaatc ggatgtagtg atatgacagg gctggggcaa gaacaggggc actagctgcc 1507 ttattagcta atttagtgcc ctccgtgttc agcttagcct ttgacccttt ccttttgatc 1567 cacaaaatac attaaaactc tgaattcaca tacaatgcta ttttaaagtc aatagatttt 1627 agctataaag tgcttgacca gtaatgtggt tgtaattttg tgtatgttcc cccacatcgc 1687 ccccaacttc ggatgtgggg tcaggaggtt gaggttcact attaacaaat gtcataaata 1747 tctcatagag gtacagtgcc aatagatatt caaatgttgc atgttgacca gagggatttt 1807 atatctgaag aacatacact attaataaat accttagaga aagattttga cctggcttta 1867 gataaaactg tggcaagaaa aatgtaatga gcaatatatg gaaataaaca cacctttgtt 1927

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<211> 1419

<212> DNA

<213> Homo sapiens

<220>

25 <221> CDS

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|     | gaagcgcc | aa gtgcgcatg | g ggacgctata | gcaattcgtt tgc  | etgteett ceteteette     | 60  |
|     | gaagatga | ca aggcctaco | a togtttotto | ctgcctttgg gcd  | egtcagge agttggttgg     | 120 |
| 5   | gacccgct | cc aaccctcg  | t tottootgos | atacagtgga tad  | caatttgt c atg gct      | 177 |
|     |          |              |              |                 | Met Ala                 |     |
|     |          |              |              | •               | 1                       |     |
|     | act ctg  | agt gtt ata  | ggt tca agt  | tca ctt att gco | c tat gct gta ttc       | 225 |
|     | Thr Leu  | Ser Val Ile  | Gly Ser Ser  | Ser Leu Ile Ala | a Tyr Ala Val Phe       |     |
| 10  |          | 5            | 10           |                 | 15                      |     |
|     | cat aat  | ata cag aaa  | tct cca gag  | ata aga cca ctt | t ttt tat ctg agc       | 273 |
|     | His Asn  | Ile Gln Lys  | Ser Pro Glu  | Ile Arg Pro Leu | ı Phe Tyr Leu Ser       |     |
|     | 20       |              | 25           | 30              | )                       |     |
|     | ttc tgt  | gac ctg ctc  | ctg gga ctt  | tgc tgg ctc acq | g gag aca ctt ctc       | 321 |
| 15  | Phe Cys  | Asp Leu Leu  | Leu Gly Leu  | Cys Trp Leu Thi | r Glu Thr Leu Leu       |     |
|     | 35       |              | 40 .         | 45              | 50                      |     |
|     |          |              |              |                 | c tat aac cta caa       | 369 |
|     | Tyr Gly  |              | Ala Asn Lys  |                 | s Tyr Asn Leu Gln       |     |
| 0.0 |          | 55           |              | 60              | 65                      |     |
| 20  |          |              |              |                 | tac acc gtc aat         | 417 |
|     | Ala Val  |              | Phe Tyr Ile  |                 | ı Tyr Thr Val Asn       |     |
|     | L-       | 70           |              | 75 ·            | 80                      |     |
|     |          |              |              |                 | a cac acc cag agt       | 465 |
| 25  | -Ar 116  | 85           | 90           | ned wid mee ply | s His Thr Gln Ser<br>95 |     |

|    | gga | cag | agc | aca | tct | cca | ctg | gtg | ata | gat | tat | act | tgt | cga | gtt | tgt | 513 |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Gly | Gln | Ser | Thr | Ser | Pro | Leu | Val | Ile | Asp | Tyr | Thr | Cys | Arg | Val | Cys |     |
|    |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |     |     |     |
|    | caa | atg | gcc | ttt | gtt | ttc | tca | agg | tgt | atc | ttg | atg | cac | tca | cca | cca | 561 |
| 5  | Gln | Met | Ala | Phe | Val | Phe | Ser | Arg | Cys | Ile | Leu | Met | His | Ser | Pro | Pro |     |
|    | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |     | 130 |     |
|    | tca | gcc | atg | gct | gaa | ctt | cca | cct | tct | gcc | aac | aca | tct | gtc | tgt | agc | 609 |
|    | Ser | Ala | Met | Ala | Glu | Leu | Pro | Pro | Ser | Ala | Asn | Thr | Ser | Val | Cys | Ser |     |
|    |     |     |     |     | 135 |     |     |     | -   | 140 |     |     |     |     | 145 |     |     |
| 10 | aca | ctt | tat | ttt | tat | ggt | atc | gcc | att | ttc | ctg | ggc | agc | ttt | gta | ctc | 657 |
|    | Thr | Leu | Tyr | Phe | Tyr | Gly | Ile | Ala | Ile | Phe | Leu | Gly | Ser | Phe | Val | Leu |     |
|    |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |     |     |     |
|    | agc | ctc | ctt | acc | att | atg | gtc | tta | ctt | atc | cga | gcc | cag | aca | ttg | tat | 705 |
|    | Ser | Leu | Leu | Thr | Ile | Met | Val | Leu | Leu | Ile | Arg | Ala | Gln | Thr | Leu | Tyr |     |
| 15 | -   |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |     |     |     |
|    | aag | aag | ttt | gtg | aag | tca | act | ggc | ttt | ctg | ggg | agt | gaa | cag | tgg | gca | 753 |
|    | Lys | Lys | Phe | Val | Lys | Ser | Thr | Gly | Phe | Leu | Gly | Ser | Glu | Gln | Trp | Ala |     |
|    |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |     |     |     |
|    | gtg | att | cac | att | gtg | gac | caa | cgg | gtg | cgc | ttc | tac | cca | gtg | gcc | ttc | 801 |
| 20 | Val | Ile | His | Ile | Val | Asp | Gln | Arg | Val | Arg | Phe | Tyr | Pro | Val | Ala | Phe |     |
|    | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |     | 210 |     |
|    | ttt | tgc | tgc | tgg | ggc | cca | gct | gtc | att | cta | atg | atc | ata | aag | ctg | act | 849 |
|    | Phe | Cys | Cys | Trp | Gly | Pro | Ala | Val | Ile | Leu | Met | Ile | Ile | Lys | Leu | Thr |     |
|    |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     | 225 |     |     |
| 25 | aag | cca | cag | gac | acc | aag | ctt | cac | atg | gcc | ctt | tat | gtt | ctc | cag | gct | 891 |

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|    | Lys  | Pro   | Gln   | Asp   | Thr   | Lys   | Leu   | His   | Met   | Ala   | Leu  | Tyr  | Val   | Leu   | Gln   | Ala    |      |
|----|------|-------|-------|-------|-------|-------|-------|-------|-------|-------|------|------|-------|-------|-------|--------|------|
|    |      |       |       | 230   |       |       |       |       | 235   |       |      |      |       | 240   |       |        |      |
|    | cta  | acg   | gca   | aca   | tct   | cag   | ggt   | cta   | ctc   | aac   | tgt  | gga  | gta   | tat   | ggc   | tgg    | 945  |
|    | Leu  | Thr   | Ala   | Thr   | Ser   | Gln   | Gly   | Leu   | Leu   | Asn   | Суѕ  | Gly  | Val   | Tyr   | Gly   | Trp    |      |
| 5  |      |       | 245   |       |       |       |       | 250   |       |       |      |      | 255   |       |       |        |      |
|    | acg  | cag   | cac   | aaa   | ttc   | cac   | caa   | cta   | aag   | cag   | gag  | gct  | cgg   | cgt   | gat   | gca    | 993  |
|    | Thr  | Gln   | His   | Lys   | Phe   | His   | Gln   | Leu   | Lys   | Gln   | Glu  | Ala  | Arg   | Arg   | Asp   | Ala    |      |
|    |      | 260   |       |       |       |       | 265   |       |       |       |      | 270  |       |       |       |        |      |
|    | gat  | acc   | cag   | aca   | cca   | tta   | tta   | tgc   | tca   | cag   | aag  | aga  | ttc   | tat   | agc   | agg    | 1041 |
| 10 | Asp  | Thr   | Gln   | Thr   | Pro   | Leu   | Leu   | Cys   | Ser   | Gln   | Lys  | Arg  | Phe   | Tyr   | Ser   | Arg    |      |
|    | 275  |       |       |       |       | 280   |       |       |       |       | 285  |      |       |       |       | 290    |      |
|    | ggc  | tta   | aat   | tca   | ctg   | gaa   | tcc   | acc   | ctg   | act   | ttt  | cct  | gcc   | agt   | act   | tct    | 1089 |
|    | Gly  | Leu   | Asn   | Ser   | Leu   | Glu   | Ser   | Thr   | Leu   | Thr   | Phe  | Pro  | Ala   | Ser   | Thr   | Ser    |      |
|    |      |       |       |       | 295   |       |       |       |       | 300   |      |      |       |       | 305   |        |      |
| 15 | acc  | att   | ttt   | tgaa  | acta  | aca a | atact | ggaa  | ac at | ccaç  | gaad | tgg  | gagtt | att   |       |        | 1138 |
|    | Thr  | Ile   | Phe   |       |       |       |       |       |       |       |      |      |       | •     |       |        |      |
|    | ctac | gcta  | at g  | gatt  | ggaa  | aa ga | aatgt | tgg   | g aaa | aggad | catc | ttaa | atct  | tt t  | tctaa | ctatg  | 1198 |
|    | ccct | aaac  | tg o  | agaa  | actca | aa ag | ggaaa | atata | a gto | gccat | tgt  | tagt | agto  | cat t | tctag | gatgaa | 1258 |
|    | ttgg | gagt  | at o  | ctctc | cagt  | t at  | tcc   | cagat | t tca | actag | gtga | tcct | taaa  | agt d | ctcta | attcag | 1318 |
| 20 | ggag | gagga | ag a  | cact  | ttco  | ca to | ctcag | gagat | aga   | actc  | gtgt | taco | ettga | atg g | gatat | tggat  | 1378 |
|    | ttgt | ctaa  | igt d | tctt  | ctag  | ga aa | aaat  | aaat  | tet   | agat  | tat  | t    |       |       |       |        | 1419 |
|    |      |       |       |       |       |       |       |       |       |       |      |      |       |       |       |        |      |
|    | <210 | )> 61 |       |       |       |       |       |       |       |       |      |      |       |       |       |        |      |
|    | <211 | .> 59 | 9     |       |       |       |       |       |       |       |      |      |       |       |       |        |      |
| 25 | <212 | ?> PF | T     |       |       |       |       |       |       |       |      |      |       |       |       |        |      |

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<213> Homo sapiens

| <1  | ^  | ^   | 61  |
|-----|----|-----|-----|
| < 1 | 11 | 115 | h i |

|    | <400 | )> 6. | L   |     |     |     |     | •   |     |     |     |     |     |     |     |     |
|----|------|-------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Met  | Pro   | Ser | Ser | Leu | Pro | Gly | Ser | Gln | Val | Pro | His | Pro | Thr | Leu | Asp |
| 5  | 1    |       |     |     | 5   |     |     |     |     | 10  |     |     | •   |     | 15  |     |
|    | Ala  | Val   | Asp | Leu | Val | Glu | Lys | Thr | Leu | Arg | Asn | Glu | Gly | Thr | Ser | Ser |
|    |      |       |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
|    | Ser  | Ala   | Pro | Val | Leu | Glu | Glu | Gly | Asp | Thr | Asp | Pro | Trp | Thr | Leu | Pro |
|    |      |       | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
| 10 | Gln  | Leu   | Lys | Asp | Thr | Ser | Gln | Pro | Trp | Lys | Glu | Leu | Arg | Val | Ala | Gly |
|    |      | 50    |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
|    | Arg  | Leu   | Arg | Arg | Val | Ala | Gly | Ser | Val | Leu | Lys | Ala | Cys | Gly | Leu | Leu |
|    | 65   |       |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
|    | Gly  | Ser   | Leu | Tyr | Phe | Phe | Ile | Cys | Ser | Leu | Asp | Val | Leu | Ser | Ser | Ala |
| 15 |      |       |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
|    | Phe  | Gln   | Leu | Leu | Gly | Ser | Lys | Val | Ala | Gly | Asp | Ile | Phe | Lys | Asp | Asn |
|    |      |       |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
|    | Val  | Val   | Leu | Ser | Asn | Pro | Val | Ala | Gly | Leu | Val | Ile | Gly | Val | Leu | Val |
|    |      |       | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
| 20 | Thr  | Ala   | Leu | Val | Gln | Ser | Ser | Ser | Thr | Ser | Ser | Ser | Ile | Val | Val | Ser |
|    |      | 130   |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
|    | Met  | Val   | Ala | Ala | Lys | Leu | Leu | Thr | Val | Arg | Val | Ser | Val | Pro | Ile | Ile |
|    | 145  |       |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
|    | Met  | Gly   | Val | Asn | Val | Gly | Thr | Ser | Ile | Thr | Ser | Thr | Leu | Val | Ser | Met |
| 25 |      |       |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |

|    | Ala | Gln | Ser | Gly | Asp | Arg | Asp | Glu | Phe | Gln | Arg | Ala | Phe | Ser | Gly | Ser |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
|    | Ala | Val | His | Gly | Ile | Phe | Asn | Trp | Leu | Thr | Val | Leu | Val | Leu | Leu | Pro |
|    |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
| 5  | Leu | Glu | Ser | Ala | Thr | Ala | Leu | Leu | Glu | Arg | Leu | Ser | Glu | Leu | Ala | Leu |
|    |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
|    | Gly | Ala | Ala | Ser | Leu | Thr | Pro | Arg | Ala | Gln | Ala | Pro | Asp | Ile | Leu | Lys |
|    | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
|    | Val | Leu | Thr | Lys | Pro | Leu | Thr | His | Leu | Ile | Val | Gln | Leu | Asp | Ser | Asp |
| 10 |     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |
|    | Met | Ile | Met | Ser | Ser | Ala | Thr | Gly | Asn | Ala | Thr | Asn | Ser | Ser | Leu | Ile |
|    |     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |
|    | Lys | His | Trp | Cys | Gly | Thr | Thr | Gly | Gln | Pro | Thr | Gln | Glu | Asn | Ser | Ser |
|    |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |
| 15 | Cys | Gly | Ala | Phe | Gly | Pro | Cys | Thr | Glu | Lys | Asn | Ser | Thr | Ala | Pro | Ala |
|    |     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |
|    | Asp | Arg | Leu | Pro | Cys | Arg | His | Leu | Phe | Ala | Gly | Thr | Glu | Leu | Thr | Asp |
|    | 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |
|    | Leu | Ala | Val | Gly | Cys | Ile | Leu | Leu | Ala | Gly | Ser | Leu | Leu | Val | Leu | Cys |
| 20 |     |     |     |     | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |
|    | Gly | Cys | Leu | Val | Leu | Ile | Val | Lys | Leu | Leu | Asn | Ser | Val | Leu | Arg | Gly |
|    |     |     |     | 340 |     |     |     |     | 345 |     |     |     |     | 350 |     |     |
|    | Arg | Val | Ala | Gln | Val | Val | Arg | Thr | Val | Ile | Asn | Ala | Asp | Phe | Pro | Phe |
|    |     |     | 355 |     |     |     |     | 360 |     |     |     |     | 365 |     |     |     |
| 25 | Pro | Leu | Gly | Trp | Leu | Gly | Gly | Tyr | Leu | Ala | Val | Leu | Ala | Gly | Ala | Gly |

|   |     |     | 370 |     |     |            |     | 375 |     |     |            |     | 380 |     |     |          |     |
|---|-----|-----|-----|-----|-----|------------|-----|-----|-----|-----|------------|-----|-----|-----|-----|----------|-----|
|   |     | Leu | Thr | Phe | Ala | Leu        | Gln | Ser | Ser | Ser | Val        | Phe | Thr | Ala | Ala | Val      | Val |
|   |     | 385 |     |     |     |            | 390 |     |     |     |            | 395 |     |     |     |          | 400 |
|   |     | Pro | Leu | Met | Gly | Val        | Gly | Val | Ile | Ser | Leu        | Asp | Arg | Ala | Tyr | Pro      | Leu |
| ! | 5   |     |     |     |     | 405        |     |     |     |     | 410        |     |     |     |     | 415      |     |
|   |     | Leu | Leu | Gly | Ser | Asn        | Ile | Gly | Thr | Thr | Thr        | Thr | Ala | Leu | Leu | Ala      | Ala |
|   |     |     |     |     | 420 |            |     |     |     | 425 |            |     |     |     | 430 |          |     |
|   |     | Leu | Ala | Ser | Pro | Ala        | Asp | Arg | Met | Leu | Ser        | Ala | Leu | Gln | Val | Ala      | Leu |
|   |     |     |     | 435 |     |            |     |     | 440 |     |            |     |     | 445 |     |          |     |
| 1 | 0   | Ile | His | Phe | Phe | Phe        | Asn | Leu | Ala | Gly | Ile        | Leu | Leu | Trp | Tyr | Leu      | Val |
|   |     |     | 450 |     |     |            |     | 455 |     |     |            |     | 460 |     |     |          |     |
|   |     | Pro | Ala | Leu | Arg | Leu        | Pro | Ile | Pro | Leu | Ala        | Arg | His | Phe | Gly | Val      | Val |
|   |     | 465 |     |     |     |            | 470 |     |     |     |            | 475 |     |     |     |          | 480 |
|   |     | Thr | Ala | Arg | Tyr | Arg        | Trp | Val | Ala | Gly | Val        | Tyr | Leu | Leu | Leu | Gly      | Phe |
| 1 | 5   |     |     |     |     | 485        |     |     |     |     | 490        |     |     |     |     | 495      |     |
|   |     | Leu | Leu | Leu | Pro | Leu        | Ala | Ala | Phe | Gly | Leu        | Ser | Leu | Ala | Gly | Gly      | Met |
|   |     |     |     |     | 500 |            |     |     |     | 505 |            |     |     |     | 510 |          |     |
|   |     | Val | Leu |     | Ala | Val        | Gly | Gly |     | Leu | Val        | Gly | Leu |     | Leu | Leu      | Val |
|   | _   |     |     | 515 |     |            |     |     | 520 |     |            |     |     | 525 |     |          |     |
| 2 | 0   | Ile |     |     | Thr | Val        | Leu |     | Arg | Arg | Arg        | Pro |     | _   | Leu | Pro      | Val |
|   |     |     | 530 |     |     |            |     | 535 | _   |     |            |     | 540 |     |     |          |     |
|   |     |     | Leu | Arg | Ser | Trp        |     | Trp | Leu | Pro | Val        |     |     | His | Ser | Leu      |     |
|   |     | 545 |     | _   | _   |            | 550 |     |     | _   |            | 555 |     | _   |     | <b>0</b> | 560 |
| 2 | 5   | Pro | тrр | Asp | Arg | Leu<br>565 |     | rnr | Arg | cys | Cys<br>570 |     | cys | Asn | vaı | Cys 575  |     |
|   | : ) |     |     |     |     | לחכ        |     |     |     |     | 5/11       |     |     |     |     | 212      |     |

144/346

Pro Pro Lys Ala Thr Thr Lys Glu Ala Tyr Cys Tyr Glu Asn Pro Glu 580 585 585 590

Ile Leu Ala Ser Gln Gln Leu

595

5

<210> 62

<211> 81

<212> PRT

<213> Homo sapiens

A.

<400> 62

10

Met Asp Gly Gl<br/>n Pro Ile Pro Ser Ser Leu Val Pro Leu Gly Asn  $\,$ 

1 5 10 15

Glu Ser Ala Asp Ser Ser Met Ser Leu Glu Gln Lys Met Thr Phe Val

15 20 25 30

Phe Val Ile Leu Leu Phe Ile Phe Leu Gly Ile Leu Ile Val Arg Cys

35 40 45

Phe Arg Ile Leu Leu Asp Pro Tyr Arg Ser Met Pro Thr Ser Thr Trp

50 55 60

20 Ala Asp Gly Leu Glu Gly Leu Glu Lys Gly Gln Phe Asp His Ala Leu

65 70 75 80

Ala

25 <210> 63

145/346

<211> 654 <212> PRT <213> Homo sapiens <400> 63 Met Ala Pro Lys Lys Leu Ser Cys Leu Arg Ser Leu Leu Leu Pro Leu Ser Leu Thr Leu Leu Pro Gln Ala Asp Thr Arg Ser Phe Val Val Asp Arg Gly His Asp Arg Phe Leu Leu Asp Gly Ala Pro Phe Arg Tyr Val Ser Gly Ser Leu His Tyr Phe Arg Val Pro Arg Val Leu Trp Ala Asp Arg Leu Leu Lys Met Arg Trp Ser Gly Leu Asn Ala Ile Gln Phe Tyr Val Pro Trp Asn Tyr His Glu Pro Gln Pro Gly Val Tyr Asn Phe Asn Gly Ser Arg Asp Leu Ile Ala Phe Leu Asn Glu Ala Ala Leu Ala Asn Leu Leu Val Ile Leu Arg Pro Gly Pro Tyr Ile Cys Ala Glu Trp Glu Met Gly Gly Leu Pro Ser Trp Leu Leu Arg Lys Pro Glu Ile His 

Leu Arg Thr Ser Asp Pro Asp Phe Leu Ala Ala Val Asp Ser Trp Phe

|    | Lys | Val | Leu | Leu | Pro | Lys | Ile | Tyr | Pro | Trp | Leu | Tyr | His | Asn | Gly | Gly |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    |     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
|    | Asn | Ile | Ile | Ser | Ile | Gln | Val | Glu | Asn | Glu | Tyr | Gly | Ser | Tyr | Arg | Ala |
|    |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
| 5  | Cys | Asp | Phe | Ser | Tyr | Met | Arg | His | Leu | Ala | Gly | Leu | Phe | Arg | Ala | Leu |
|    |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
|    | Leu | Gly | Glu | Lys | Ile | Leu | Leu | Phe | Thr | Thr | Asp | Gly | Pro | Glu | Gly | Leu |
| •  |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
|    | Lys | Cys | Gly | Ser | Leu | Arg | Gly | Leu | Tyr | Thr | Thr | Val | Asp | Phe | Gly | Pro |
| 10 | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
|    | Ala | Asp | Asn | Met | Thr | Lys | Ile | Phe | Thr | Leu | Leu | Arg | Lys | Tyr | Glu | Pro |
|    |     |     |     |     | 245 |     |     |     |     | 250 | ,   |     |     |     | 255 |     |
|    | His | Gly | Pro | Leu | Val | Asn | Ser | Glu | Tyr | Tyr | Thr | Gly | Trp | Leu | Asp | Tyr |
|    |     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |
| 15 | Trp | Gly | Gln | Asn | His | Ser | Thr | Arg | Ser | Val | Ser | Ala | Val | Thr | Lys | Gly |
|    |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |
|    | Leu | Glu | Asn | Met | Leu | Lys | Leu | Gly | Ala | Ser | Val | Asn | Met | Tyr | Met | Phe |
|    |     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |
|    | His | Gly | Gly | Thr | Asn | Phe | Gly | Tyr | Trp | Asn | Gly | Ala | Asp | Lys | Lys | Gly |
| 20 | 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |
|    | Arg | Phe | Leu | Pro | Ile | Thr | Thr | Ser | Tyr | Asp | Tyr | Asp | Ala | Pro | Ile | Ser |
|    |     |     |     |     | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |
|    | Glu | Ala | Gly | Asp | Pro | Thr | Pro | Lys | Leu | Phe | Ala | Leu | Arg | Asp | Val | Ile |
|    |     |     |     | 340 |     |     |     |     | 345 |     |     |     |     | 350 |     |     |
| 25 | Ser | Lys | Phe | Gln | Glu | Val | Pro | Leu | Gly | Pro | Leu | Pro | Pro | Pro | Ser | Pro |

|    |     |     | 355 |     |     |     |     | 360 |     |     |     |     | 365 |     |     |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Lys | Met | Met | Leu | Gly | Pro | Val | Thr | Leu | His | Leu | Val | Gly | His | Leu | Leu |
|    |     | 370 |     |     |     |     | 375 |     |     |     |     | 380 |     |     |     |     |
|    | Ala | Phe | Leu | Asp | Leu | Leu | Cys | Pro | Arg | Gly | Pro | Ile | His | Ser | Ile | Leu |
| 5  | 385 |     |     |     |     | 390 |     |     |     |     | 395 |     |     |     |     | 400 |
|    | Pro | Met | Thr | Phe | Glu | Ala | Val | Lys | Gln | Asp | His | Gly | Phe | Met | Leu | Tyr |
|    |     |     |     |     | 405 |     |     |     |     | 410 |     |     |     |     | 415 |     |
|    | Arg | Thr | Tyr | Met | Thr | His | Thr | Ile | Phe | Glu | Pro | Thr | Pro | Phe | Trp | Val |
|    |     |     |     | 420 |     |     |     |     | 425 |     |     |     |     | 430 |     |     |
| 10 | Pro | Asn | Asn | Gly | Val | His | Asp | Arg | Ala | Tyr | Val | Met | Val | Asp | Gly | Val |
|    |     |     | 435 |     |     |     |     | 440 |     |     |     |     | 445 |     |     |     |
|    | Phe | Gln | Gly | Val | Val | Glu | Arg | Asn | Met | Arg | Asp | Lys | Leu | Phe | Leu | Thr |
|    |     | 450 |     |     |     |     | 455 |     |     |     |     | 460 |     |     |     |     |
|    | Gly | Lys | Leu | Gly | Ser | Lys | Leu | Asp | Ile | Leu | Val | Glu | Asn | Met | Gly | Arg |
| 15 | 465 |     |     |     |     | 470 |     |     |     |     | 475 |     |     |     |     | 480 |
|    | Leu | Ser | Phe | Gly | Ser | Asn | Ser | Ser | Asp | Phe | Lys | Gly | Leu | Leu | Lys | Pro |
|    |     |     |     |     | 485 |     |     |     |     | 490 |     |     |     |     | 495 |     |
|    | Pro | Ile | Leu | Gly | Gln | Thr | Ile | Leu | Thr | Gln | Trp | Met | Met | Phe | Pro | Leu |
|    |     |     |     | 500 |     |     |     |     | 505 |     |     |     |     | 510 |     |     |
| 20 | Lys | Ile | Asp | Asn | Leu | Val | Lys | Trp | Trp | Phe | Pro | Leu | Gln | Leu | Pro | Lys |
|    |     |     | 515 |     |     |     |     | 520 |     |     |     |     | 525 |     |     |     |
|    | Trp | Pro | Tyr | Pro | Gln | Ala | Pro | Ser | Gly | Pro | Thr | Phe | Tyr | Ser | Lys | Thr |
|    |     | 530 |     |     |     |     | 535 |     |     |     |     | 540 |     |     |     |     |
|    | Phe | Pro | Ile | Leu | Gly | Ser | Val | Gly | Asp | Thr | Phe | Leu | Tyr | Leu | Pro | Gly |
| 25 | 545 |     |     |     |     | 550 |     |     |     |     | 555 |     |     |     |     | 560 |

|      | Trp  | Thr   | Lys   | Gly   | Gln | Val | Trp | Ile | Asn | Gly | Phe | Asn | Leu | Gly | Arg | Tyr |
|------|------|-------|-------|-------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|      |      |       |       |       | 565 |     |     |     |     | 570 |     |     |     |     | 575 |     |
|      | Trp  | Thr   | Lys   | Gln   | Gly | Pro | Gln | Gln | Thr | Leu | Tyr | Val | Pro | Arg | Phe | Leu |
|      |      |       |       | 580   |     |     |     |     | 585 |     |     |     |     | 590 |     |     |
| 5    | Leu  | Phe   | Pro   | Arg   | Gly | Ala | Leu | Asn | Lys | Ile | Thr | Leu | Leu | Glu | Leu | Glu |
|      |      |       | 595   |       |     |     |     | 600 |     |     |     |     | 605 |     |     |     |
|      | Asp  | Val   | Pro   | Leu   | Gln | Pro | Gln | Val | Gln | Phe | Leu | Asp | Lys | Pro | Ile | Leu |
|      |      | 610   |       |       |     |     | 615 |     |     |     |     | 620 |     |     |     |     |
|      | Asn  | Ser   | Thr   | Ser   | Thr | Leu | His | Arg | Thr | His | Ile | Asn | Ser | Leu | Ser | Ala |
| 10 . | 625  |       |       |       |     | 630 |     |     |     |     | 635 |     |     |     |     | 640 |
|      | Asp  | Thr   | Leu   | Ser   | Ala | Ser | Glu | Pro | Met | Glu | Leu | Ser | Gly | His |     |     |
|      |      |       |       |       | 645 |     |     |     |     | 650 |     |     |     |     |     |     |
|      |      |       |       |       |     |     |     |     |     |     |     |     |     |     |     |     |
|      | <210 | )> 64 | 1     |       |     |     |     |     | -   |     |     |     |     | ٠   |     |     |
| 15   | <211 | L> 39 | 90    |       |     |     |     |     |     |     |     |     |     |     |     |     |
|      | <212 | ?> PF | RT    |       |     |     |     |     |     |     |     |     |     |     |     |     |
|      | <213 | 3> нс | omo s | sapie | ens |     |     |     |     |     |     |     |     |     |     |     |
|      |      |       |       |       |     |     |     |     |     |     |     |     |     |     |     |     |
|      | <400 | )> 64 | 1     |       |     |     |     |     |     |     |     |     |     |     |     |     |
| 20   | Met  | Gly   | Met   | Asp   | Asp | Cys | Asp | Ser | Phe | Phe | Pro | Gly | Pro | Leu | Val | Ala |
|      | 1    |       |       |       | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
|      | Ile  | Ile   | Cys   | Asp   | Ile | Leu | Gly | Glu | Lys | Thr | Thr | Ser | Ile | Leu | Gly | Ala |
|      |      |       |       | 20    |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
|      | Phe  | Val   | Val   | Thr   | Gly | Gly | Tyr | Leu | Ile | Ser | Ser | Trp | Ala | Thr | Ser | Ile |
| 25   |      |       | 35    |       |     |     |     | 40  |     | •   |     |     | 45  |     |     |     |

|    | Pro | Phe | Leu | Cys | Val | Thr | Met | Gly | Leu | Leu | Pro | Gly | Leu  | Gly | Ser | Ala |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|-----|-----|-----|
|    |     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |      |     |     |     |
|    | Phe | Leu | Tyr | Gln | Val | Ala | Ala | Val | Val | Thr | Thr | Lys | Tyr  | Phe | Lys | Lys |
|    | 65  |     |     |     |     | 70  |     |     |     |     | 75  |     | •    |     |     | 80  |
| 5  | Arg | Leu | Ala | Leu | Ser | Thr | Ala | Ile | Ala | Arg | Ser | Gly | Met  | Gly | Leu | Thr |
|    |     |     |     |     | 85  |     | •   |     |     | 90  |     |     | •    |     | 95  |     |
|    | Phe | Leu | Leu | Ala | Pro | Phe | Thr | Lys | Phe | Leu | Ile | Asp | Leu  | Tyr | Asp | Trp |
|    |     |     |     | 100 |     |     |     |     | 105 |     |     |     |      | 110 |     |     |
|    | Thr | Gly | Ala | Leù | Ile | Leu | Phe | Gly | Ala | Ile | Ala | Leu | Asn  | Leu | Val | Pro |
| 10 |     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125  |     |     |     |
|    | Ser | Ser | Met | Leu | Leu | Arg | Pro | Ile | His | Ile | Lys | Ser | Glu  | Asn | Asn | Ser |
|    |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |      |     |     |     |
|    | Gly | Ile | Lys | Asp | Lys | Gly | Ser | Ser | Leu | Ser | Ala | His | Gly  | Pro | Glu | Ala |
|    | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |      |     |     | 160 |
| 15 | His | Alạ | Thr | Glu | Thr | His | Суз | His | Glu | Thr | Glu | Glu | Ser  | Thr | Ile | Lys |
|    |     |     |     |     | 165 |     |     |     |     | 170 |     |     |      |     | 175 |     |
|    | Asp | Ser | Thr | Thr | Gln | Lys | Ala | Gly | Leu | Pro | Ser | Lys | Asn  | Leu | Thr | Val |
|    |     |     |     | 180 |     |     |     |     | 185 |     |     |     |      | 190 |     |     |
|    | Ser | Gln | Asn | Gln | Ser | Glu | Glu | Phe | Tyr | Asn | Gly | Pro | Asn  | Arg | Asn | Arg |
| 20 |     |     | 195 |     |     | •   |     | 200 |     |     |     |     | 205  |     |     |     |
|    | Leu | Leu | Leu | Lys | Ser | Asp | Glu | Glu | Ser | Asp | Lys | Val | 'Ile | Ser | Trp | Ser |
|    |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |      |     |     |     |
|    | Cys | Lys | Gln | Leu | Phe | Asp | Ile | Ser | Leu | Phe | Arg | Asn | Pro  | Phe | Phe | Tyr |
|    | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |      |     |     | 240 |
| 25 | Ile | Phe | Thr | Trp | Ser | Phe | Leu | Leu | Ser | Gln | Leu | Ala | Tyr  | Phe | Ile | Pro |

|    |      |       |       |       | 245   |     |     |     |     | 250 |     |     |     |     | 255 |     |
|----|------|-------|-------|-------|-------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Thr  | Phe   | His   | Leu   | Val   | Ala | Arg | Ala | Lys | Thr | Leu | Gly | Ile | Asp | Ile | Met |
|    |      |       |       | 260   |       |     |     |     | 265 |     |     |     |     | 270 |     |     |
|    | Asp  | Ala   | Ser   | Tyr   | Leu   | Val | Ser | Val | Ala | Gly | Ile | Leu | Glu | Thr | Val | Sei |
| 5  |      |       | 275   |       |       |     |     | 280 |     |     |     |     | 285 |     |     |     |
|    | Gln  | Ile   | Ile   | Ser   | Gly   | Trp | Val | Ala | Asp | Gln | Asn | Trp | Ile | Lys | Lys | Туг |
|    |      | 290   |       |       |       |     | 295 |     |     |     |     | 300 |     |     |     |     |
|    | His  | Tyr   | His   | Lys   | Ser   | Tyr | Leu | Ile | Leu | Cys | Gly | Ile | Thr | Asn | Leu | Let |
|    | 305  |       |       |       |       | 310 |     |     |     |     | 315 |     |     |     |     | 320 |
| 10 | Ala  | Pro   | Leu   | Ala   | Thr   | Thr | Phe | Pro | Leu | Leu | Met | Thr | Tyr | Thr | Ile | Cys |
|    |      |       |       |       | 325   |     |     |     |     | 330 |     |     |     |     | 335 |     |
|    | Phe  | Ala   | Ile   | Phe   | Ala   | Gly | Gly | Tyr | Leu | Ala | Leu | Ile | Leu | Pro | Val | Leu |
|    |      |       |       | 340   |       |     |     |     | 345 |     | •   |     |     | 350 |     |     |
|    | Val  | Asp   | Leu   | Cys   | Arg   | Asn | Ser | Thr | Val | Asn | Arg | Phe | Leu | Gly | Leu | Ala |
| 15 |      |       | 355   |       |       |     |     | 360 |     |     |     |     | 365 |     |     |     |
|    | Ser  | Phe   | Phe   | Ala   | Gly   | Met | Ala | Val | Leu | Ser | Gly | Pro | Pro | Ile | Ala | Gly |
|    |      | 370   |       | 4     |       |     | 375 |     |     |     |     | 380 |     |     |     |     |
|    | Asn  | Thr   | Phe   | Thr   | Thr   | Phe |     |     |     |     |     |     |     |     |     |     |
|    | 385  |       |       |       |       | 390 |     |     |     |     |     |     |     |     |     |     |
| 20 |      |       |       |       |       |     |     |     |     |     |     |     |     |     |     |     |
|    | <210 | )> 65 | 5     |       |       |     |     |     |     |     |     |     |     |     |     |     |
|    | <211 | L> 45 | 52    |       |       |     |     |     |     |     |     |     |     |     |     |     |
|    | <212 | ?> PF | RT.   |       |       |     |     |     |     |     |     |     |     |     |     |     |
|    | <213 | 3> Ho | omo s | sapie | ens . |     |     |     |     |     |     |     |     |     |     |     |
| 25 |      |       |       |       |       |     |     |     |     |     |     |     |     |     |     |     |

|     | <400 | )> 65 | •     |       |       |     |         |       |      |     |     |     |       |     |     |     |
|-----|------|-------|-------|-------|-------|-----|---------|-------|------|-----|-----|-----|-------|-----|-----|-----|
|     | Met  | Glu   | Leu   | Ala   | Leu   | Arg | Arg     | Ser   | Pro  | Val | Pro | Arg | Trp   | Leu | Leu | Leu |
|     | 1    |       |       |       | 5     |     |         |       |      | 10  |     |     |       |     | 15  |     |
|     | Leu  | Pro   | Leu   | Leu   | Leu   | Gly | Leu     | Asn   | Ala  | Gly | Ala | Val | Ile   | Asp | Trp | Pro |
| 5   |      |       |       | 20    |       |     |         |       | 25   |     |     |     |       | 30  |     |     |
|     | Thr  | Glu   | Glu   | Gly   | Lys   | Glu | Val     | Trp   | Asp  | Tyr | Val | Thr | Val   | Arg | Lys | Asp |
|     |      |       | 35    |       |       |     |         | 40    |      |     |     |     | 45    |     |     |     |
|     | Ala  | Tyr   | Met   | Phe   | Trp   | Trp | Leu     | Tyr   | Tyr  | Ala | Thr | Asn | Ser   | Cys | Lys | Asn |
|     |      | 50    |       |       |       |     | 55      |       |      |     |     | 60  |       |     |     |     |
| 10  | Phe  | Ser   | Glu   | Leu   | Pro   | Leu | Val     | Met   | Trp  | Leu | Gln | Gly | Gly   | Pro | Gly | Gly |
|     | 65   |       |       |       |       | 70  |         |       |      |     | 75  |     | ,     |     |     | 80  |
|     | Ser  | Ser   | Thr   | Gly   | Phe   | Gly | Asn     | Phe   | Glu. | Glu | Ile | Gly | Pro   | Leu | Asp | Ser |
|     |      |       |       |       | 85    |     |         |       |      | 90  |     |     |       |     | 95  |     |
|     | Asp  | Leu   | Lys   | Pro   | Arg   | Lys | Thr     | Thr   | Trp  | Leu | Gln | Ala | Ala   | Ser | Leu | Leu |
| 15  |      |       |       | 100   |       |     |         |       | 105  |     |     |     |       | 110 |     |     |
|     | Phe  | Val   | Asp   | Asn   | Pro   | Val | Gly     | Thr   | Gly  | Phe | Ser | Tyr | Val   | Asn | Gly | Ser |
|     |      |       | 115   |       |       |     |         | 120   |      |     |     |     | 125   |     |     |     |
|     | Gly  | Ala   | Tyr   | Ala   | Lys   | Asp | Leu     | Ala   | Met  | Val | Ala | Ser | Asp   | Met | Met | Val |
|     |      | 130   |       |       |       |     | 135     |       |      |     |     | 140 |       |     |     |     |
| 20  | Leu  | Lev   | Lys   | Thr   | Phe   | Phe | Ser     | Cys   | His  | Lys | Glu | Phe | Gln   | Thr | Val | Pro |
|     | 145  |       |       |       |       | 150 |         |       |      |     | 155 |     |       |     |     | 160 |
|     | Phe  | Tyr   | : Ile | Phe   | Ser   | Glu | ser Ser | Tyr   | Gly  | Gly | Lys | Met | Ala   | Ala |     | Ile |
|     |      |       |       |       | 165   |     |         |       |      | 170 |     |     |       |     | 175 |     |
|     | Gl   | / Let | ı Glu | ı Lev | 1 Туі | Lys | s Ala   | ı Ile | Gln  | Arg | Gly | Thr | : Ile |     |     | Asn |
| 2.5 |      |       |       | 100   | ,     |     |         |       | 105  |     |     |     |       | 190 |     |     |

|    | Phe | Ala | Gly | Val | Ala | Leu | Gly | Asp | Ser | Trp | Ile | Ser | Pro        | Val | Asp | Ser |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------------|-----|-----|-----|
|    |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205        |     |     |     |
|    | Val | Leu | Ser | Trp | Gly | Pro | Tyr | Leu | Tyr | Ser | Met | Ser | Leu        | Leu | Glu | Asp |
|    |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |            |     |     |     |
| 5  | Lys | Gly | Leu | Ala | Glu | Val | Ser | Lys | Val | Ala | Glu | Gln | Val        | Leu | Asn | Ala |
|    | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |            |     |     | 240 |
|    | Val | Asn | Lys | Gly | Leu | Tyr | Arg | Glu | Ala | Thr | Glu | Leu | Trp        | Gly | Lys | Ala |
|    |     |     |     |     | 245 |     |     |     |     | 250 |     |     |            |     | 255 |     |
|    | Glu | Met | Ile | Ile | Glu | Gln | Asn | Thr | Asp | Gly | Val | Asn | Phe        | Tyr | Asn | Ile |
| 10 |     |     |     | 260 |     |     |     |     | 265 |     | ٠   |     |            | 270 |     |     |
|    | Leu | Thr | Lys | Ser | Thr | Pro | Thr | Ser | Thr | Met | Glu | Ser | Ser        | Leu | Glu | Phe |
|    |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285        |     |     |     |
|    | Thr | Gln | Ser | His | Leu | Val | Суз | Leu | Cys | Gln | Arg | His | Val        | Arg | His | Leu |
|    |     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |            |     |     |     |
| 15 | Gln | Arg | Asp | Ala | Leu | Ser | Gln | Leu | Met | Asn | Gly | Pro | Ile        | Arg | Lys | Lys |
|    | 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |            | ,   |     | 320 |
|    | Leu | Lys | Ile | Ile | Pro | Glu | Asp | Gln | Ser | Trp | Gly | Gly | Gln        | Ala | Thr | Asn |
|    |     |     |     |     | 325 |     |     |     |     | 330 |     |     |            |     | 335 |     |
|    | Val | Phe | Val | Asn | Met | Glu | Glu | Asp | Phe | Met | Lys | Pro | Val        | Ile | Ser | Ile |
| 20 |     |     |     | 340 |     |     |     |     | 345 |     |     |     |            | 350 |     |     |
|    | Val | Asp | Glu | Leu | Leu | Glu | Ala | Gly | Ile | Asn | Val | Thr | <b>Val</b> | Tyr | Asn | Gly |
|    |     |     | 355 |     |     |     |     | 360 |     |     |     |     | 365        |     |     |     |
|    | Gln | Leu | Asp | Leu | Ile | Val | Asp | Thr | Met | Gly | Gln | Glu | Ala        | Trp | Val | Arg |
|    |     | 370 |     |     |     |     | 375 |     |     |     |     | 380 |            |     |     |     |
| 25 | Lys | Leu | Lys | Trp | Pro | Glu | Leu | Pro | Lys | Phe | Ser | Gln | Leu        | Lys | Trp | Lys |

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Ala Leu Tyr Ser Asp Pro Lys Ser Leu Glu Thr Ser Ala Phe Val Lys Ser Tyr Lys Asn Leu Ala Phe Tyr Trp Ile Leu Lys Ala Gly His Met Val Pro Ser Asp Gln Gly Asp Met Ala Leu Lys Met Met Arg Leu Val Thr Gln Gln Glu <210> 66 <211> 490 <212> PRT <213> Homo sapiens <400> 66 Met Arg Pro Ala Phe Ala Leu Cys Leu Leu Trp Gln Ala Leu Trp Pro Gly Pro Gly Gly Glu His Pro Thr Ala Asp Arg Ala Gly Cys Ser Ala Ser Gly Ala Cys Tyr Ser Leu His His Ala Thr Met Lys Arg Gln Ala Ala Glu Glu Ala Cys Ile Leu Arg Gly Gly Ala Leu Ser Thr Val Arg Ala Gly Ala Glu Leu Arg Ala Val Leu Ala Leu Leu Arg Ala Gly

|    | 65   |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
|----|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Pro  | Gly | Pro | Gly | Gly | Gly | Ser | Lys | Asp | Leu | Leu | Phe | Trp | Val | Ala | Leu |
|    |      |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
|    | Glu  | Arg | Arg | Arg | Ser | His | Cys | Thr | Leu | Glu | Asn | Glu | Pro | Leu | Arg | Gly |
| 5  |      |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
|    | Phe  | Ser | Trp | Leu | Ser | Ser | Asp | Pro | Gly | Gly | Leu | Glu | Ser | Asp | Thr | Leu |
|    |      |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
|    | Gln  | Trp | Val | Glu | Glu | Pro | Gln | Arg | Ser | Cys | Thr | Ala | Arg | Arg | Cys | Ala |
|    |      | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
| 10 | ·Val | Leu | Gln | Ala | Thr | Gly | Gly | Val | Glu | Pro | Ala | Gly | Trp | Lys | Glu | Met |
|    | 145  |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
|    | Arg  | Cys | His | Leu | Arg | Ala | Asn | Gly | Tyr | Leu | Суз | Lys | Tyr | Gln | Phe | Glu |
|    |      |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
|    | Val  | Leu | Cys | Pro | Ala | Pro | Arg | Pro | Gly | Ala | Ala | Ser | Asn | Leu | Ser | Tyr |
| 15 |      |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
|    | Arg  | Ala | Pro | Phe | Gln | Leu | His | Ser | Ala | Ala | Leu | Asp | Phe | Ser | Pro | Pro |
|    |      |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
|    | Gly  | Thr | Glu | Val | Ser | Ala | Leu | Cys | Arg | Gly | Gln | Leu | Pro | Ile | Ser | Val |
|    |      | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
| 20 | Thr  | Cys | Ile | Ala | Asp | Glu | Ile | Gly | Ala | Arg | Trp | Asp | Lys | Leu | Ser | Gly |
|    | 225  |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
|    | Asp  | Val | Leu | Cys | Pro | Cys | Pro | Gly | Arg | Tyr | Leu | Arg | Ala | Gly | Lys | Cys |
|    |      |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |
|    | Ala  | Glu | Leu | Pro | Asn | Cys | Leu | Asp | Asp | Leu | Gly | Gly | Phe | Ala | Cys | Glu |
| 25 |      |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |

|    | Суѕ | Ala | Thr | Gly | Phe | Glu | Leu | Gly | Lys | Asp | Gly | Arg | Ser | Cys | Val | Thr |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |
|    | Ser | Gly | Glu | Gly | Gln | Pro | Thr | Leu | Gly | Gly | Thr | Gly | Val | Pro | Thr | Arg |
|    |     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |
| 5  | Arg | Pro | Pro | Ala | Thr | Ala | Thr | Ser | Pro | Val | Pro | Gln | Arg | Thr | Trp | Pro |
|    | 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |
|    | Ile | Arg | Val | Asp | Glu | Lys | Leu | Gly | Gļu | Thr | Pro | Leu | Val | Pro | Glu | Gln |
|    |     |     |     |     | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |
|    | Asp | Asn | Ser | Val | Thr | Ser | Ile | Pro | Glu | Ile | Pro | Arg | Trp | Gly | Ser | Gln |
| 10 |     |     |     | 340 |     |     |     | ,   | 345 |     |     |     |     | 350 |     | •   |
| •  | Ser | Thr | Met | Ser | Thr | Leu | Gln | Met | Ser | Leu | Gln | Ala | Glu | Ser | Lys | Ala |
|    |     |     | 355 |     |     |     |     | 360 |     |     |     |     | 365 |     |     |     |
|    | Thr | Ile | Thr | Pro | Ser | Gly | Ser | Val | Ile | Ser | Lys | Phe | Asn | Ser | Thr | Thr |
|    |     | 370 |     |     |     |     | 375 |     |     |     |     | 380 |     |     |     |     |
| 15 | Ser | Ser | Ala | Thr | Pro | Gln | Ala | Phe | Asp | Ser | Ser | Ser | Ala | Val | Val | Phe |
|    | 385 |     |     |     |     | 390 |     |     |     |     | 395 |     |     |     |     | 400 |
|    | Ile | Phe | Val | Ser | Thr | Ala | Val | Val | Val | Leu | Val | Íle | Leu | Thr | Met | Thr |
|    |     |     |     |     | 405 |     |     |     |     | 410 |     |     |     |     | 415 |     |
|    | Val | Leu | Gly | Leu | Val | Lys | Leu | Cys | Phe | His | Glu | Ser | Pro | Ser | Ser | Gln |
| 20 |     |     |     | 420 |     |     |     |     | 425 |     |     |     |     | 430 |     |     |
|    | Pro | Arg | Lys | Glu | Ser | Met | Gly | Pro | Pro | Gly | Leu | Glu | Ser | Asp | Pro | Glu |
|    |     |     | 435 |     |     |     |     | 440 |     |     |     |     | 445 |     |     |     |
|    | Pro | Ala | Ala | Leu | Gly | Ser | Ser | Ser | Ala | His | Суз | Thr | Asn | Asn | Gly | Val |
|    |     | 450 |     |     |     |     | 455 |     |     |     |     | 460 |     |     |     |     |
| 25 | Lys | Val | Gly | Asp | Cys | Asp | Leu | Arg | Asp | Arg | Ala | Glu | Gly | Ala | Leu | Leu |

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Ala Glu Ser Pro Leu Gly Ser Ser Asp Ala .490 <210> 67 <211> 392 <212> PRT <213> Homo sapiens <400> 67 Met Gln Val Asn Thr Thr Lys Phe Met Leu Leu Tyr Ala Trp Tyr Ser Trp Pro Asn Val Val Leu Cys Phe Phe Gly Gly Phe Leu Ile Asp Arg Val Phe Gly Ile Arg Trp Gly Thr Ile Ile Phe Ser Cys Phe Val Cys Ile Gly Gln Val Val Phe Ala Leu Gly Gly Ile Phe Asn Ala Phe Trp Leu Met Glu Phe Gly Arg Phe Val Phe Gly Ile Gly Gly Glu Ser Leu Ala Val Ala Gln Asn Thr Tyr Ala Val Ser Trp Phe Lys Gly Lys Glu Leu Asn Leu Val Phe Gly Leu Gln Leu Ser Met Ala Arg Ile Gly Ser Thr Val Asn Met Asn Leu Met Gly Trp Leu Tyr Ser Lys Ile Glu Ala

|    |     |     | 115 |         |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
|----|-----|-----|-----|---------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Leu | Leu | Gly | Ser     | Ala | Gly | His | Thr | Thr | Leu | Gly | Ile | Thr | Leu | Met | Ile |
|    |     | 130 |     |         |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
|    | Gly | Gly | Ile | Thr     | Cys | Ile | Leu | Ser | Leu | Ile | Cys | Ala | Leu | Ala | Leu | Ala |
| 5  | 145 |     |     |         |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
|    | Tyr | Leu | Asp | Gln     | Arg | Ala | Glu | Arg | Ile | Leu | His | Lys | Glu | Gln | Gly | Lys |
|    |     |     |     |         | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
|    | Thr | Gly | Glu | Val     | Ile | Lys | Leu | Thr | Asp | Val | Lys | Asp | Phe | Ser | Leu | Pro |
|    |     |     |     | 180     |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
| 10 | Leu | Trp | Leu | Ile     | Phe | Ile | Ile | Cys | Val | Cys | Tyr | Tyr | Val | Ala | Val | Phe |
|    |     |     | 195 |         |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
|    | Pro | Phe | Ile | Gly     | Leu | Gly | Lys | Val | Phe | Phe | Thr | Glu | Lys | Phe | Gly | Phe |
|    |     | 210 |     |         |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
|    | Ser | Ser | Gln | <br>Ala | Ala | Ser | Ala | Ile | Asn | Ser | Val | Val | Tyr | Val | Ile | Ser |
| 15 | 225 |     |     |         |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
|    | Ala | Pro | Met | Ser     | Pro | Val | Phe | Gly | Leu | Leu | Val | Asp | Lys | Thr | Gly | Lys |
|    |     |     |     |         | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |
|    | Asn | Ile | Ile | Trp     | Val | Leu | Cys | Ala | Val | Ala | Ala | Thr | Leu | Val | Ser | His |
|    |     |     |     | 260     |     |     |     |     | 265 |     |     |     |     | 270 |     |     |
| 20 | Met | Met | Leu | Ala     | Phe | Thr | Met | Trp | Asn | Pro | Trp | Ile | Ala | Met | Cys | Leu |
|    |     |     | 275 |         |     |     |     | 280 |     |     |     |     | 285 |     |     |     |
|    | Leu | Gly | Leu | Ser     | Tyr | Ser | Leu | Leu | Ala | Cys | Ala | Leu | Trp | Pro | Met | Val |
|    |     | 290 |     |         |     |     | 295 |     |     |     |     | 300 |     |     |     |     |
|    | Ala | Phe | Val | Val     | Pro | Glu | His | Gln | Leu | Gly | Thr | Ala | Tyr | Gly | Phe | Met |
| 25 | 305 |     |     |         |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |

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Gln Ser Ile Gln Asn Leu Gly Leu Ala Ile Ile Ser Ile Ile Ala Gly Met Ile Leu Asp Ser Arg Gly Tyr Leu Phe Leu Glu Val Phe Phe Ile Ala Cys Val Ser Leu Ser Leu Leu Ser Val Val Leu Leu Tyr Leu Val Asn Arg Ala Gln Gly Gly Asn Leu Asn Tyr Ser Ala Arg Gln Arg Glu Glu Ile Lys Phe Ser His Thr Glu <210> 68 <211> 538 <212> PRT <213> Homo sapiens <400> 68 Met Gly Cys Leu Trp Gly Leu Ala Leu Pro Leu Phe Phe Phe Cys Trp Glu Val Gly Val Ser Gly Ser Ser Ala Gly Pro Ser Thr Arg Arg Ala Asp Thr Ala Met Thr Thr Asp Asp Thr Glu Val Pro Ala Met Thr Leu Ala Pro Gly His Ala Ala Leu Glu Thr Gln Thr Leu Ser Ala Glu Thr 

|    | Ser | Ser | Arg | Ala | Ser | Thr | Pro | Ala | Gly      | Pro | Ile | Pro | Glu | Ala | Glu | Thr |
|----|-----|-----|-----|-----|-----|-----|-----|-----|----------|-----|-----|-----|-----|-----|-----|-----|
|    | 65  |     |     |     |     | 70  |     |     |          |     | 75  |     |     |     |     | 80  |
|    | Arg | Gly | Ala | Lys | Arg | Ile | Ser | Pro | Ala      | Arg | Glu | Thr | Arg | Ser | Phe | Thr |
|    |     |     |     |     | 85  |     |     |     |          | 90  |     |     |     |     | 95  |     |
| 5  | Lys | Thr | Ser | Pro | Asn | Phe | Met | Val | Leu      | Ile | Ala | Thr | Ser | Val | Glu | Thr |
|    |     |     |     | 100 |     |     |     |     | 105      |     |     |     |     | 110 |     |     |
|    | Ser | Ala | Ala | Ser | Gly | Ser | Pro | Glu | Gly<br>· | Ala | Gly | Met | Thr | Thr | Val | Gln |
|    |     |     | 115 |     |     |     |     | 120 |          |     |     |     | 125 |     |     |     |
|    | Thr | lle | Thr | Gly | Ser | Asp | Pro | Glu | Glu      | Ala | Ile | Phe | Asp | Thr | Leu | Cys |
| 10 |     | 130 |     |     |     |     | 135 |     |          |     |     | 140 |     |     |     |     |
|    | Thr | Asp | Asp | Ser | Ser | Glu | Glu | Ala | Lys      | Thr | Leu | Thr | Met | Asp | Ile | Leu |
|    | 145 |     |     |     |     | 150 |     |     |          |     | 155 |     |     |     |     | 160 |
|    | Thr | Leu | Ala | His | Thr | Ser | Thr | Glu | Ala      | Lys | Gly | Leu | Ser | Ser | Glu | Ser |
|    |     |     |     |     | 165 |     |     |     |          | 170 |     |     |     |     | 175 |     |
| 15 | Ser | Ala | Ser | Ser | Asp | Gly | Pro | His | Pro      | Val | Ile | Thr | Pro | Ser | Arg | Ala |
|    |     |     |     | 180 |     |     |     |     | 185      |     |     |     |     | 190 |     |     |
|    | Ser | Glu | Ser | Ser | Ala | Ser | Ser | Asp | Gly      | Pro | His | Pro | Val | Ile | Thr | Pro |
|    |     |     | 195 |     |     |     |     | 200 |          |     |     |     | 205 |     |     |     |
|    | Ser | Arg | Ala | Ser | Glu | Ser | Ser | Ala | Ser      | Ser | Asp | Gly | Pro | His | Pro | ۷al |
| 20 |     | 210 |     |     |     |     | 215 |     |          |     |     | 220 |     |     |     |     |
|    | Ile | Thr | Pro | Ser | Trp | Ser | Pro | Gly | Ser      | Asp | Val | Thr | Leu | Leu | Ala | Glu |
|    | 225 |     |     |     |     | 230 |     |     |          |     | 235 |     |     |     |     | 240 |
|    | Ala | Leu | Val | Thr | Val | Thr | Asn | Ile | Glu      | Val | Ile | Asn | Cys | Ser | Ile | Thr |
|    |     |     |     |     | 245 |     |     |     |          | 250 |     |     |     |     | 255 |     |
| 25 | Glu | Ile | Glu | Thr | Thr | Thr | Ser | Ser | Ile      | Pro | Gly | Ala | Ser | Asp | Ile | Asp |

|    |     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Leu | Ile | Pro | Thr | Glu | Gly | Val | Lys | Ala | Ser | Ser | Thr | Ser | Asp | Pro | Pro |
|    |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |
|    | Ala | Leu | Pro | Asp | Ser | Thr | Glu | Ala | Lys | Pro | His | Ile | Thr | Glu | Val | Thr |
| 5  |     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |
|    | Ala | Ser | Ala | Glu | Thr | Leu | Ser | Thr | Ala | Gly | Thr | Thr | Glu | Ser | Ala | Ala |
|    | 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |
|    | Pro | His | Ala | Thr | Val | Gly | Thr | Pro | Leu | Pro | Thr | Asn | Ser | Ala | Thr | Glu |
|    |     |     |     |     | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |
| 10 | Arg | Glu | Val | Thr | Ala | Pro | Gly | Ala | Thr | Thr | Leu | Ser | Gly | Ala | Leu | Val |
|    |     |     |     | 340 |     |     |     |     | 345 |     |     |     |     | 350 |     |     |
|    | Thr | Val | Ser | Arg | Asn | Pro | Leu | Glu | Glu | Thr | Ser | Ala | Leu | Ser | Val | Glu |
|    |     |     | 355 |     |     |     |     | 360 |     |     |     |     | 365 |     |     |     |
|    | Thr | Pro | Ser | Tyr | Val | Lys | Val | Ser | Gly | Ala | Ala | Pro | Val | Ser | Ile | Glu |
| 15 |     | 370 |     |     |     |     | 375 |     |     |     |     | 380 |     |     |     |     |
|    | Ala | Gly | Ser | Ala | Val | Gly | Lys | Thr | Thr | Ser | Phe | Ala | Gly | Ser | Ser | Ala |
|    | 385 |     |     |     |     | 390 |     |     |     |     | 395 |     |     |     |     | 400 |
|    | Ser | Ser | Tyr | Ser | Pro | Ser | Glu | Ala | Ala | Leu | Lys | Asn | Phe | Thr | Pro | Ser |
|    |     |     |     |     | 405 |     |     |     |     | 410 |     |     |     |     | 415 |     |
| 20 | Glu | Thr | Pro | Thr | Met | Asp | Ile | Ala | Thr | Lys | Gly | Pro | Phe | Pro | Thr | Ser |
|    |     |     |     | 420 |     |     |     |     | 425 |     |     |     |     | 430 |     |     |
|    | Arg | Asp | Pro | Leu | Pro | Ser | Val | Pro | Pro | Thr | Thr | Thr | Asn | Ser | Ser | Arg |
|    |     |     | 435 |     |     |     |     | 440 |     |     |     |     | 445 |     |     |     |
|    | Gly | Thr | Asn | Ser | Thr | Leu | Ala | Lys | Ile | Thr | Thr | Ser | Ala | Lys | Thr | Thr |
| 25 |     | 450 |     |     |     |     | 455 |     |     |     |     | 460 |     |     |     |     |

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Met Lys Pro Pro Thr Ala Thr Pro Thr Thr Ala Arg Thr Arg Pro Thr Thr Asp Val Ser Ala Gly Glu Asn Gly Gly Phe Leu Leu Leu Arg Leu Ser Val Ala Ser Pro Glu Asp Leu Thr Asp Pro Arg Val Ala Glu Arg Leu Met Gln Gln Leu His Arg Glu Leu His Ala His Ala Pro His Phe Gln Val Ser Leu Leu Arg Val Arg Arg Gly <210> 69 <211> 102 <212> PRT <213> Homo sapiens <400> 69 Met Glu Ala Ala Leu Leu Gly Leu Cys Asn Trp Ser Thr Leu Gly Val Cys Ala Ala Leu Lys Leu Pro Gln Ile Ser Ala Val Leu Ala Ala Arg Ser Ala Arg Gly Leu Ser Leu Pro Ser Leu Leu Leu Glu Leu Ala Gly Phe Leu Val Phe Leu Arg Tyr Gln Cys Tyr Tyr Gly Tyr Pro Pro Leu 

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Thr Tyr Leu Glu Tyr Pro Ile Leu Ile Ala Gln Asp Val Ile Leu Leu Leu Cys Ile Phe His Phe Asn Gly Asn Val Lys Gln Ala Thr Pro Tyr Ile Ala Val Tyr Pro Phe <210> 70 <211> 442 <212> PRT <213> Homo sapiens <400> 70 Met Gly Leu Ala Met Glu His Gly Gly Ser Tyr Ala Arg Ala Gly Gly Ser Ser Arg Gly Cys Trp Tyr Tyr Leu Arg Tyr Phe Phe Leu Phe Val Ser Leu Ile Gln Phe Leu Ile Ile Leu Gly Leu Val Leu Phe Met Val Tyr Gly Asn Val His Val Ser Thr Glu Ser Asn Leu Gln Ala Thr Glu Arg Arg Ala Glu Gly Leu Tyr Ser Gln Leu Leu Gly Leu Thr Ala Ser Gln Ser Asn Leu Thr Lys Glu Leu Asn Phe Thr Thr Arg Ala Lys Asp 

|    | Ala | Ile | Met | Gln | Met | Trp | Leu | Asn | Ala | Arg | Arg | Asp | Leu | Asp | Arg | Ile |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    |     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
|    | Asn | Ala | Ser | Phe | Arg | Gln | Cys | Gln | Gly | Asp | Arg | Val | Ile | Tyr | Thr | Asr |
|    |     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
| 5  | Asn | Gln | Arg | Tyr | Met | Ala | Ala | Ile | Ile | Leu | Ser | Glu | Lys | Gln | Cys | Arc |
|    |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
|    | Asp | Gln | Phe | Lys | Asp | Met | Asn | Lys | Ser | Cys | Asp | Ala | Leu | Leu | Phe | Met |
|    | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
|    | Leu | Asn | Gln | Lys | ۷al | Lys | Thr | Leu | Glu | Val | Glu | Ile | Ala | Lys | Glu | Lys |
| 10 |     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
|    | Thr | Ile | Cys | Thr | Lys | Asp | Lys | Glu | Ser | Val | Leu | Leu | Asn | Lys | Arg | ۷a۱ |
|    |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
|    | Ala | Glu | Glu | Gln | Leu | Val | Glu | Cys | Val | Lys | Thr | Arg | Glu | Leu | Gln | His |
|    |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
| 15 | Gln | Glu | Arg | Gln | Leu | Ala | Lys | Glu | Gln | Leu | Gln | Lys | Val | Gln | Ala | Let |
|    |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
|    | Cys | Leu | Pro | Leu | Asp | Lys | Asp | Lys | Phe | Glu | Met | Asp | Leu | Arg | Asn | Lev |
|    | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
|    | Trp | Arg | Asp | Ser | Ile | Ile | Pro | Arg | Ser | Leu | Asp | Asn | Leu | Gly | Tyr | Asr |
| 20 |     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |
|    | Leu | Tyr | His | Pro | Leu | Gly | Ser | Glu | Leu | Ala | Ser | Ile | Arg | Arg | Ala | Cys |
|    |     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |
|    | Asp | His | Met | Pro | Ser | Leu | Met | Ser | Ser | Lys | Val | Glu | Glu | Leu | Ala | Arg |
|    |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |
| 25 | Ser | Leu | Arg | Ala | Asp | Ile | Glu | Arg | Val | Ala | Arg | Glu | Asn | Ser | Asp | Leu |

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G

Gln Arg Gln Lys Leu Glu Ala Gln Gln Gly Leu Arg Ala Ser Gln Glu Ala Lys Gln Lys Val Glu Lys Glu Ala Gln Ala Arg Glu Ala Lys Leu Gln Ala Glu Cys Ser Arg Gln Thr Gln Leu Ala Leu Glu Glu Lys Ala Val Leu Arg Lys Glu Arg Asp Asn Leu Ala Lys Glu Leu Glu Glu Lys Lys Arg Glu Ala Glu Gln Leu Arg Met Glu Leu Ala Ile Arg Asn Ser Ala Leu Asp Thr Cys Ile Lys Thr Lys Ser Gln Pro Met Met Pro Val Ser Arg Pro Met Gly Pro Val Pro Asn Pro Gln Pro Ile Asp Pro Ala Ser Leu Glu Glu Phe Lys Arg Lys Ile Leu Glu Ser Gln Arg Pro Pro Ala Gly Ile Pro Val Ala Pro Ser Ser Gly <210> 71 <211> 1800 <212> DNA

<213> Homo sapiens

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<400> 71

5

10

15

20

25

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accepted acceptaged georgogy taccetaged teggatect georgece 1500 ctggegget tegggetete cetggeaggg ggeatggtee teggegetet egggggteee 1560 ctggtgggge teggtgeteet egteateetg gttactgtee tegageggeg eeggeeggee 1620 teggetgeetg teeggeetge eteetgggee teggeteee tetggeteea teetgggge 1680 ceetgggaee geetggtgae eegetgetge eeetgeaaeg tetgeageee eeeggagee 1740 accaecaaag aggeetaetg etaegagaae eetgagatet teggeteeea geagttgtga 1800

<210> 72

<211> 246

10 <212> DNA

5

<213> Homo sapiens

<400> 72

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ttgggcattc tcattgtccg gtgcttccgg attcttttgg atccatatcg aagcatgcca 180

acctctacct gggctgatgg acttgaaggc ctggagaaag ggcagttcga ccatgccctt 240

gcttag 246

20 <210> 73

<211> 1965

<212> DNA

<213> Homo sapiens

25 <400> 73

5

10

15

20

25

#### 167/346

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tactecaaaa cattteeaat tttaggetea gttggggaca catttetata tetacetgga 1680
tggaccaagg geeaagtetg gateaatggg tttaaettgg geeggtaetg gacaaageag 1740
gggeeacaac agacceteta egtgeeaaga tteetgetgt tteetagggg ageeeteaac 1800
aaaattacat tgetggaact agaagatgta eeteteeage eecaagteea attttggat 1860
aageetatee teaatageae tagtaetttg eacaggacae atateaatte eettteaget 1920
gatacactga gtgeetetga accaatggag ttaagtggge actga 1965

10 <210> 74

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<211> 1173

<212> DNA

<213> Homo sapiens

15 <400> 74

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atatttactt ggtetttet ceteagteag ttageatact teatecetae ettteacetg 780
gtageeagag ccaaaacact ggggattgac ateatggatg cetettacet tgtttetgta 840

geaggtatee ttgagaeggt cagteagat atttetggat gggttgetga teaaaactgg 900
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getggtggtt acetggeatt gatactgeet gtaetggttg atetggtag gaattetaca 1080
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<210> 75

<211> 1359

<212> DNA

15 <213> Homo sapiens

<400> 75

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25

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<210> 76

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15

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<211> 1473

<212> DNA

20 <213> Homo sapiens

<400> 76

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caccaegeta eeatgaageg geaggeggee gaggaggeet geateetgeg aggtggggeg 180

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|    | ctcagcaccg | tgcgtgcggg | cgccgagctg | cgcgctgtgc | tcgcgctcct | gcgggcaggc | 240  |
|----|------------|------------|------------|------------|------------|------------|------|
|    | ccagggcccg | gagggggctc | caaagacctg | ctgttctggg | tcgcactgga | gcgcaggcgt | 300  |
|    | tcccactgca | ccctggagaa | cgagcctttg | cggggtttct | cctggctgtc | ctccgacccc | 360  |
|    | ggcggtctcg | aaagcgacac | gctgcagtgg | gtggaggagc | cccaacgctc | ctgcaccgcg | 420  |
| 5  | cggagatgcg | cggtactcca | ggccaccggt | ggggtcgagc | ccgcaggctg | gaaggagatg | 480  |
|    | cgatgccacc | tgcgcgccaa | cggctacctg | tgcaagtacc | agtttgaggt | cttgtgtcct | 540  |
|    | gegeegegee | ceggggeege | ctctaacttg | agctatcgcg | cgcccttcca | gctgcacagc | 600  |
|    | gccgctctgg | acttcagtcc | acctgggacc | gaggtgagtg | cgctctgccg | gggacagctc | 660  |
|    | ccgatctcag | ttacttgcat | cgcggacgaa | atcggcgctc | gctgggacaa | actctcgggc | 720  |
| 10 | gatgtgttgt | gtccctgccc | cgggaggtac | ctccgtgctg | gcaaatgcgc | agageteect | 780  |
|    | aactgcctag | acgacttggg | aggctttgcc | tgcgaatgtg | ctacgggctt | cgagctgggg | 840  |
|    | aaggacggcc | gctcttgtgt | gaccagtggg | gaaggacagc | cgacccttgg | ggggaccggg | 900  |
|    | gtgcccacca | ggcgcccgcc | ggccactgca | accagccccg | tgccgcagag | aacatggcca | 960  |
|    | atcagggtcg | acgagaagct | gggagagaca | ccacttgtcc | ctgaacaaga | caattcagta | 1020 |
| 15 | acatctattc | ctgagattcc | tcgatgggga | tcacagagca | cgatgtctac | ccttcaaatg | 1080 |
|    | tcccttcaag | ccgagtcaaa | ggccactatc | accccatcag | ggagcgtgat | ttccaagttt | 1140 |
|    | aattctacga | cttcctctgc | cactcctcag | gctttcgact | cctcctctgc | cgtggtcttc | 1200 |
|    | atatttgtga | gcacagcagt | agtagtgttg | gtgatcttga | ccatgacagt | actggggctt | 1260 |
|    | gtcaagctct | gctttcacga | aagcccctct | tcccagccaa | ggaaggagtc | tatgggcccg | 1320 |
| 20 | ccgggcctgg | agagtgatcc | tgagcccgct | gctttgggct | ccagttctgc | acattgcaca | 1380 |
|    | aacaatgggg | tgaaagtcgg | ggactgtgat | ctgcgggaca | gagcagaggg | tgccttgctg | 1440 |
|    | gcggagtccc | ctcttggctc | tagtgatgca | tag        |            |            | 1473 |

<210> 77

25 <211> 1179

#### 172/346

<212> DNA

<213> Homo sapiens

<400> 77

5

10

15

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20

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<210> 78

<211> 1617

<212> DNA

<213> Homo sapiens

5

10

15

20

25

<400> 78

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teetectaca geeeetegga ageegeeete aagaacttea eeeetteaga gacacegace 1260
atggacateg caaccaaggg geeetteeee accageaggg accetettee ttetgteeet 1320
cegactacaa eeaacageag eegagggaeg aacageacet tageeaagat cacaacetea 1380
gegaagacea egatgaagee eeeaacagee acgeeeacga etgeeeggae gaggeegaee 1440
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tatccgccgc tgacctacct ggagtacccc atcctcatcg cgcaagatgt catcctcctg 240
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#### 175/346

#### <213> Homo sapiens

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176/346

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Met Pro Ser Ser Leu Pro Gly Ser Gln Val Pro

1 5 10

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Glu Gly Thr Ser Ser Ser Ala Pro Val Leu Glu Gly Asp Thr Asp

30 35 4

ccc tgg acc ctc cct cag ctg aag gac aca agc cag ccc tgg aaa gag 254
Pro Trp Thr Leu Pro Gln Leu Lys Asp Thr Ser Gln Pro Trp Lys Glu

25 45 50 55

|    | ctc | cgc | gtg | gcc | ggc   | agg | ctg | cgc | cgc | gtg  | gcc | ggc | agc | gtc | ctc | aag | 302   |
|----|-----|-----|-----|-----|-------|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|-----|-------|
|    | Leu | Arg | Val | Ala | Gly   | Arg | Leu | Arg | Arg | Val  | Ala | Gly | Ser | Val | Leu | Lys |       |
|    | 60  |     |     | ٠   |       | 65  |     |     |     |      | 70  |     |     |     |     | 75  |       |
|    | gcc | tgc | ggg | ctc | ctc   | ggc | agc | ctg | tac | ttc  | ttc | atc | tgc | tct | ctg | gac | 350   |
| 5  | Ala | Cys | Gly | Leu | Leu   | Gly | Ser | Leu | Tyr | Phe  | Phe | Ile | Cys | Ser | Leu | Asp |       |
|    |     |     |     |     | 80    |     |     |     |     | 85   |     |     |     |     | 90  |     |       |
|    | gtc | ctc | agc | tcc | gcc   | ttc | cag | ctg | ctg | ggc  | agc | aaa | gtg | gcc | gga | gac | 398   |
|    | Val | Leu | Ser | Ser | Ala   | Phe | Gln | Leu | Leu | Gly  | Ser | Lys | Val | Ala | Gly | Asp |       |
|    |     |     |     | 95  |       |     |     |     | 100 |      |     |     |     | 105 |     |     |       |
| 10 | atc | ttc | aag | gac | aac   | gtg | gtg | ctg | tcc | aac  | cct | gtg | gct | gga | ctg | gtc | . 446 |
|    | Ile | Phe | Lys | Asp | Asn   | Val | Val | Leu | Ser | Asn  | Pro | Val | Ala | Gly | Leu | Val |       |
|    |     |     | 110 |     |       |     |     | 115 |     |      |     |     | 120 |     |     |     |       |
|    | att | ggc | gtg | ctg | gtc   | aca | gcc | ctg | gtg | cag  | agt | tcc | agc | acg | tcc | tcc | 494   |
|    | Ile | Gly | Val | Leu | Val   | Thr | Ala | Leu | Val | Gln  | Ser | Ser | Ser | Thr | Ser | Ser |       |
| 15 |     | 125 |     |     |       |     | 130 |     |     |      |     | 135 |     |     |     |     |       |
|    | tcc | atc | gtg | gtc | agc   | atg | gtg | gct | gct | aag  | ctg | ctg | act | gtc | cgg | gtg | 542   |
|    | Ser | Ile | Val | Val | Ser   | Met | Val | Ala | Ala | Lys  | Leu | Leu | Thr | Val | Arg | Val |       |
|    | 140 | ٠   |     |     |       | 145 |     |     |     |      | 150 |     |     |     |     | 155 |       |
|    | tct | gtg | ccc | atc | atc   | atg | ggt | gtc | aac | gta  | ggc | aca | tcc | atc | acc | agc | 590   |
| 20 | Ser | Val | Pro | Ile | Ile   | Met | Gly | Val | Asn | 'Val | Gly | Thr | Ser | Ile | Thr | Ser |       |
|    |     |     |     |     | 160   |     |     |     |     | 165  |     |     |     |     | 170 |     |       |
|    | acc | ctg | gto | tca | atg   | gcg | cag | tca | ggg | gac  | cgg | gat | gaa | ttt | cag | agg | 638   |
|    | Thr | Leu | Val | Ser | Met   | Ala | Gln | Ser | Gly | Asp  | Arg | Asp | Glu | Phe | Gln | Arg |       |
|    |     |     |     | 175 | •     |     |     |     | 180 |      |     |     |     | 185 |     |     |       |
| 25 | gct | tto | ago | ggc | : tcg | gcg | gtg | cac | ggg | ato  | ttc | aac | tgg | ctc | aca | gtg | 686   |

|    | Ala | Phe | Ser | Gly | Ser | Ala | Val | His | Gly | Ile | Phe | Asn | Trp | Leu | Thr | Val   |      |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------|------|
|    |     |     | 190 |     |     |     |     | 195 |     |     |     |     | 200 |     |     |       |      |
|    | ctg | gtc | ctg | ctg | cca | ctg | gag | agc | gcc | acg | gcc | ctg | ctg | gag | agg | cta   | 734  |
|    | Leu | Val | Leu | Leu | Pro | Leu | Glu | Ser | Ala | Thr | Ala | Leu | Leu | Glu | Arg | Leu   |      |
| 5  |     | 205 |     |     |     |     | 210 |     |     |     |     | 215 |     |     |     |       |      |
|    | agt | gag | cta | gcc | ctg | ggt | gcc | gcc | agc | ctg | aca | ccc | agg | gcg | cag | gcg   | 782  |
|    | Ser | Glu | Lẹu | Ala | Leu | Gly | Ala | Ala | Ser | Leu | Thr | Pro | Arg | Ala | Gln | Ala   |      |
|    | 220 |     |     |     |     | 225 |     |     |     |     | 230 |     |     |     |     | 235   |      |
|    | ccc | gac | atc | ctc | aag | gtg | ctg | acg | aag | ccg | ctc | aca | cac | ctc | atc | gtg   | 830  |
| 10 | Pro | Asp | Ile | Leu | Lys | Val | Leu | Thr | Lys | Pro | Leu | Thr | His | Leu | Ile | Val   |      |
|    |     |     |     |     | 240 |     |     |     |     | 245 |     |     |     |     | 250 |       |      |
|    | cag | ctg | gac | tcc | gac | atg | atc | atg | agc | agt | gcc | aca | ggc | aac | gcc | act   | 878  |
|    | Gln | Leu | Asp | Ser | Asp | Met | Ile | Met | Ser | Ser | Ala | Thr | Gly | Asn | Ala | Thr   |      |
|    |     |     |     | 255 |     |     |     |     | 260 |     |     |     |     | 265 |     |       |      |
| 15 | aac | agc | agt | ctc | att | aag | cac | tgg | tgc | ggc | acc | acg | äää | cag | ccg | acc   | 926  |
|    | Asn | Ser | Ser | Leu | Ile | Lys | His | Trp | Cys | Gly | Thr | Thr | Gly | Gln | Pro | Thr   | 4    |
| `  |     |     | 270 |     |     |     |     | 275 |     |     |     |     | 280 |     |     |       |      |
|    | cag | gag | aac | agc | agc | tgt | ggc | gcc | ttc | ggc | ccg | tgc | aca | gag | aag | aac   | 974  |
|    | Gln | Glu | Asn | Ser | Ser | Cys | Gly | Ala | Phe | Gly | Pro | Cys | Thr | Glu | Lys | Asn   |      |
| 20 |     | 285 |     |     |     |     | 290 |     |     |     |     | 295 |     |     |     |       |      |
|    | agc | aca | gcc | ccg | gcg | gac | agg | ctg | ccc | tgc | cgc | cac | ctg | ttt | gcg | ggc   | 1022 |
|    | Ser | Thr | Ala | Pro | Ala | Asp | Arg | Leu | Pro | Cys | Arg | His | Leu | Phe | Ala | Gly   |      |
|    | 300 |     |     |     |     | 305 |     |     |     |     | 310 |     |     |     |     | 315   |      |
|    | acg | gag | ctc | acg | gac | ctg | gcc | gtg | ggc | tgc | atc | ctg | ctg | gcc | ggc | tcc . | 1070 |
| 25 | Thr | Glu | Leu | Thr | Asp | Leu | Ala | Val | Gly | Cys | Ile | Leu | Leu | Ala | Gly | Ser   |      |

|    |     | •   |     |     | 320 |     |     |     |     | 325 |     |     |     |     | 330 |     |      |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|    | ctg | ctg | gtg | ctc | tgc | ggc | tgc | ctg | gtc | ctc | ata | gtc | aag | ctg | ctc | aac | 1118 |
|    | Leu | Leu | Val | Leu | Cys | Gly | Cys | Leu | Val | Leu | Ile | Val | Lys | Leu | Leu | Asn |      |
|    |     |     |     | 335 |     |     |     |     | 340 |     |     |     |     | 345 |     |     |      |
| 5  | tct | gtg | ctg | cgc | ggc | cgc | gtg | gcc | cag | gtc | gtg | agg | aca | gtc | atc | aat | 1166 |
|    | Ser | Val | Leu | Arg | Gly | Arg | Val | Ala | Gln | Val | Val | Arg | Thr | Val | Ile | Asn |      |
|    |     |     | 350 |     |     |     |     | 355 |     |     |     |     | 360 |     |     |     |      |
|    | gcg | gac | ttc | ccc | ttc | ccg | ctg | ggc | tgg | ctc | ggc | ggc | tac | ctg | gcc | gtc | 1214 |
|    | Ala | Asp | Phe | Pro | Phe | Pro | Leu | Gly | Trp | Leu | Gly | Gly | Tyr | Leu | Ala | Val |      |
| 10 |     | 365 |     |     |     |     | 370 |     |     |     |     | 375 |     |     |     |     |      |
|    | ctc | gcg | ggc | gcc | ggc | ctg | acc | ttc | gca | ctg | cag | agc | agc | agc | gtc | ttc | 1262 |
|    | Leu | Ala | Gly | Ala | Gly | Leu | Thr | Phe | Ala | Leu | Gln | Ser | Ser | Ser | Val | Phe |      |
|    | 380 |     |     |     |     | 385 |     |     |     |     | 390 |     |     |     |     | 395 |      |
|    | acg | gcg | gcc | gtc | gtg | ccc | ctc | atg | ggg | gtc | ggg | gtg | atc | agt | ctg | gac | 1310 |
| 15 | Thr | Ala | Ala | Val | Val | Pro | Leu | Met | Gly | Val | Gly | Val | Ile | Ser | Leu | Asp |      |
|    |     |     |     |     | 400 |     |     |     |     | 405 |     |     |     |     | 410 |     |      |
|    | cgg | gcg | tac | ccc | ctc | tta | ctg | ggc | tcc | aac | atc | ggc | acc | act | acc | aca | 1358 |
|    | Arg | Ala | Tyr | Pro | Leu | Leu | Leu | Gly | Ser | Asn | Ile | Gly | Thr | Thr | Thr | Thr |      |
|    |     |     |     | 415 |     |     |     |     | 420 |     |     |     |     | 425 |     |     |      |
| 20 | gcc | ctg | ctg | gct | gcc | ctg | gcc | agc | ccc | gca | gac | agg | atg | ctc | agc | gcc | 1406 |
|    | Ala | Leu | Leu | Ala | Ala | Leu | Ala | Ser | Pro | Ala | Asp | Arg | Met | Leu | Ser | Ala |      |
|    |     |     | 430 |     |     |     |     | 435 |     |     |     |     | 440 |     |     |     |      |
|    | ctg | cag | gtc | gcc | ctc | atc | cac | ttc | ttc | ttc | aac | ctg | gcc | ggc | atc | ctg | 1454 |
|    | Leu | Gln | Val | Ala | Leu | Ile | His | Phe | Phe | Phe | Asn | Leu | Ala | Gly | Ile | Leu |      |
| 25 |     | 445 |     |     |     |     | 450 |     |     |     |     | 455 |     |     |     |     |      |

|    | ctg | tgg | tac | ctg | gtg | cct | gca | ctg | cgg | ctg | ccc | atc | ccg | ctg  | gcc   | agg | 1502 |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|-------|-----|------|
|    | Leu | Trp | Tyr | Leu | Val | Pro | Ala | Leu | Arg | Leu | Pro | Ile | Pro | Leu  | Ala   | Arg |      |
|    | 460 |     |     |     |     | 465 |     |     |     |     | 470 |     |     |      |       | 475 |      |
|    | cac | ttc | ggg | gtg | gtg | acc | gcc | cgt | tac | cgc | tgg | gtg | gct | ggg  | gtc   | tac | 1550 |
| 5  | His | Phe | Gly | Val | Val | Thr | Ala | Arg | Tyr | Arg | Trp | Val | Ala | Gly  | Ϋal   | Tyr |      |
|    |     |     |     |     | 480 |     |     |     |     | 485 |     |     |     |      | 490   |     |      |
|    | ctg | ctg | ctc | gga | ttc | ctg | ctg | ctg | ccc | ctg | gcg | gcc | ttc | ggg  | ctc   | tcc | 1598 |
|    | Leu | Leu | Leu | Gly | Phe | Leu | Leu | Leu | Pro | Leu | Ala | Ala | Phe | Gly  | Leu   | Ser |      |
|    |     |     |     | 495 |     |     |     |     | 500 |     |     |     |     | 505  |       |     |      |
| 10 | ctg | gca | ggg | ggc | atg | gtg | ctg | gcc | gct | gtc | ggg | ggt | ccc | ctg  | gtg   | ggg | 1646 |
|    | Leu | Ala | Gly | Gly | Met | Val | Leu | Ala | Ala | Val | Gly | Gly | Pro | Leu  | Val   | Gly |      |
|    |     |     | 510 |     |     |     |     | 515 |     |     |     |     | 520 |      |       |     |      |
|    | ctg | gtg | ctc | ctc | gtc | atc | ctg | gtt | act | gtc | ctg | cag | cgg | cgc  | cgg   | ccg | 1694 |
|    | Leu | Val | Leu | Leu | Val | Ile | Leu | Val | Thr | Val | Leu | Gln | Arg | Arg  | Arg   | Pro | •    |
| 15 |     | 525 |     |     |     |     | 530 | •   |     |     |     | 535 |     |      |       |     |      |
|    | gcc | tgg | ctg | cct | gtc | cgc | ctg | cgc | tcc | tgg | gcc | tgg | ctc | ccc  | gtc   | tgg | 1742 |
|    | Ala | Trp | Leu | Pro | Val | Arg | Leu | Arg | Ser | Trp | Ala | Trp | Leu | Pro  | Val   | Trp |      |
|    | 540 |     |     |     |     | 545 |     |     |     |     | 550 |     |     |      |       | 555 |      |
|    | ctc | cat | tct | ctg | gag | ccc | tgg | gac | cgc | ctg | gtg | acc | cgc | tgc  | tgc   | ccc | 1790 |
| 20 | Leu | His | Ser | Leu | Glu | Pro | Trp | Asp | Arg | Leu | Val | Thr | Arg | Cys  | Cys   | Pro |      |
|    |     |     |     |     | 560 |     |     |     |     | 565 |     |     |     |      | 570   |     |      |
|    | tgc | aac | gtc | tgc | agc | ccc | ccg | aag | gcc | acc | acc | aaa | gag | gcc  | tac   | tgc | 1838 |
|    | Cys | Asn | Val | Cys | Ser | Pro | Pro | Lys | Ala | Thr | Thr | Lys | Glu | Ala  | Tyr   | Cys |      |
|    |     |     |     | 575 |     |     |     |     | 580 |     |     |     |     | 585  |       |     |      |
| 25 | tac | gag | aac | cct | gag | atc | ttg | gcc | tcc | caq | caq | tta | tga | caad | gcagt | tq  | 1887 |

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Tyr Glu Asn Pro Glu Ile Leu Ala Ser Gln Gln Leu

590 595 600

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aaaccaggat atcctgtgct ctggcttccc tggacc atg gat gga gga cag ccc 354
Met Asp Gly Gly Gln Pro

. 5

atc ccc tca tcc cta gtg ccc ctt ggg aac gaa tca gca gat tct agc 402

25 Ile Pro Ser Ser Leu Val Pro Leu Gly Asn Glu Ser Ala Asp Ser Ser

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| taggttgcaa | gtgcagctta | aagtttttt  | tcaatgaaaa | gttaattgtt | tagaggagaa | 1372 |
|------------|------------|------------|------------|------------|------------|------|
| gacttttata | gtcttcagag | gaatgtgtat | ttatgattgt | atatagtcac | caaataaaac | 1432 |
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<222> (40)..(2004)

<400> 83

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Met Ala Pro Lys Lys

1 5

ctg tcc tgc ctt cgt tcc ctg ctg ctg ccg ctc agc ctg acg cta ctg 102
Leu Ser Cys Leu Arg Ser Leu Leu Pro Leu Ser Leu Thr Leu Leu

20 10 15 20

ctg ccc cag gca gac act cgg tcg ttc gta gtg gat agg ggt cat gac 150
Leu Pro Gln Ala Asp Thr Arg Ser Phe Val Val Asp Arg Gly His Asp

25 30 35

cgg ttt ctc cta gac ggg gcc ccg ttc cgc tat gtg tct ggc agc ctg 198

25 Arg Phe Leu Leu Asp Gly Ala Pro Phe Arg Tyr Val Ser Gly Ser Leu

|    |     |     | 40  |     |     |     |     | 45  |      |     |     |     | 50  |     |     |     |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|-----|-----|-----|
|    | cac | tac | ttt | cgg | gta | ccg | cgg | gtg | ctt  | tgg | gcc | gac | cgg | ctt | ttg | aag | 246 |
|    | His | Tyr | Phe | Arg | Val | Pro | Arg | Val | Leu  | Trp | Ala | Asp | Arg | Leu | Leu | Lys |     |
|    |     | 55  |     |     |     |     | 60  |     |      |     |     | 65  |     |     |     |     |     |
| 5  | atg | cga | tgg | agc | ggc | ctc | aac | gcc | ata  | cag | ttt | tat | gtg | ccc | tgg | aac | 294 |
|    | Met | Arg | Trp | Ser | Gly | Leu | Asn | Ala | Ile  | Gln | Phe | Tyr | Val | Pro | Trp | Asn |     |
| •  | 70  |     |     |     |     | 75  |     |     |      |     | 80  |     |     |     |     | 85  |     |
|    | tac | cac | gag | cca | cag | cct | ggg | gtc | tat. | aac | ttt | aat | ggc | agc | cgg | gac | 342 |
|    | Tyr | His | Glu | Pro | Gln | Pro | Gly | Val | Tyr  | Asn | Phe | Asn | Gly | Ser | Arg | Asp |     |
| 10 |     |     |     |     | 90  |     |     |     |      | 95  |     |     |     |     | 100 | -   |     |
|    | ctc | att | gcc | ttt | ctg | aat | gag | gca | gct  | cta | gcg | aac | ctg | ttg | gtc | ata | 390 |
|    | Leu | Ile | Ala | Phe | Leu | Asn | Glu | Ala | Ala  | Leu | Ala | Asn | Leu | Leu | Val | Ile |     |
|    |     |     |     | 105 |     |     |     |     | 110  |     |     |     |     | 115 |     |     |     |
|    | ctg | aga | cca | gga | cct | tac | atc | tgt | gca  | gag | tgg | gag | atg | ggg | ggt | ctc | 438 |
| 15 | Leu | Arg | Pro | Gly | Pro | Tyr | Ile | Cys | Ala  | Glu | Trp | Glu | Met | Gly | Gly | Leu |     |
|    |     |     | 120 |     |     |     |     | 125 |      |     |     |     | 130 |     |     |     | •   |
|    | cca | tcc | tgg | ttg | ctt | cga | aaa | cct | gaa  | att | cat | cta | aga | acc | tca | gat | 486 |
|    | Pro | Ser | Trp | Leu | Leu | Arg | Lys | Pro | Glu  | Ile | His | Leu | Arg | Thr | Ser | Asp |     |
|    |     | 135 |     |     |     |     | 140 |     |      |     |     | 145 |     |     |     |     |     |
| 20 | cca | gac | ttc | ctt | gcc | gca | gtg | gac | tcc  | tgg | ttc | aag | gtc | ttg | ctg | ccc | 534 |
|    | Pro | Asp | Phe | Leu | Ala | Ala | Val | Asp | Ser  | Trp | Phe | Lys | Val | Leu | Leu | Pro |     |
|    | 150 |     |     |     |     | 155 |     |     |      |     | 160 |     |     |     |     | 165 |     |
|    | aag | ata | tat | cca | tgg | ctt | tat | cac | aat  | ggg | ggc | aac | atc | att | agc | att | 582 |
|    | Lys | Ile | Tyr | Pro | Trp | Leu | Tyr | His | Asn  | Gly | Gly | Asn | Ile | Ile | Ser | Ile |     |
| 25 |     |     |     |     | 170 |     |     |     |      | 175 |     |     |     |     | 180 |     |     |

|    | cag | gtg | gag | aat | gaa | tat | ggt | agc | tac              | aga | gcc | tgt | gac | ttc | agc | tac | 630  |
|----|-----|-----|-----|-----|-----|-----|-----|-----|------------------|-----|-----|-----|-----|-----|-----|-----|------|
|    | Gln | Val | Glu | Asn | Glu | Tyr | Gly | Ser | Tyr              | Arg | Ala | Cys | Asp | Phe | Ser | Tyr |      |
|    |     |     |     | 185 |     |     |     |     | 190              |     |     |     |     | 195 |     |     |      |
|    | atg | agg | cac | ttg | gct | ggg | ctc | ttc | cgt              | gca | ctg | cta | gga | gaa | aag | atc | 678  |
| 5  | Met | Arg | His | Leu | Ala | Gly | Leu | Phe | Arg              | Ala | Leu | Leu | Gly | Glu | Lys | Ile |      |
|    |     |     | 200 |     |     |     |     | 205 |                  |     |     |     | 210 |     |     |     |      |
|    | ttg | ctc | ttc | acc | aca | gat | ggg | cct | gaa              | gga | ctc | aag | tgt | ggc | tcc | ctc | 726  |
|    | Leu | Leu | Phe | Thr | Thr | Asp | Gly | Pro | Glu              | Gly | Leu | Lys | Cys | Gly | Ser | Leu |      |
|    |     | 215 |     |     |     |     | 220 |     |                  |     |     | 225 |     |     |     |     |      |
| 10 | cgg | gga | ctc | tat | acc | act | gta | gat | ttt              | ggc | cca | gct | gac | aac | atg | acc | 774  |
|    | Arg | Gly | Leu | Tyr | Thr | Thr | Val | Asp | Phe              | Gly | Pro | Ala | Asp | Asn | Met | Thr |      |
|    | 230 |     |     |     |     | 235 |     |     |                  |     | 240 |     |     |     |     | 245 |      |
|    | aaa | atc | ttt | acc | ctg | ctt | cgg | aag | tat              | gaa | ccc | cat | ggg | cca | ttg | gta | 822  |
|    | Lys | Ile | Phe | Thr | Leu | Leu | Arg | Lys | Tyr              | Glu | Pro | His | Gly | Pro | Leu | Val |      |
| 15 |     |     |     |     | 250 |     |     |     |                  | 255 |     |     |     |     | 260 |     |      |
|    | aac | tct | gag | tac | tac | aca | ggc | tgg | ctg              | gat | tac | tgg | ggc | cag | aat | cac | 870  |
|    | Asn | Ser | Glu | Tyr | Tyr | Thr | Gly | Trp | Leu              | Asp | Tyr | Trp | Gly | Gln | Asn | His |      |
|    |     |     |     | 265 |     |     |     |     | 270 <sup>.</sup> |     |     |     |     | 275 |     |     |      |
|    | tcc | aca | cgg | tct | gtg | tca | gct | gta | acc              | aaa | gga | cta | gag | aac | atg | ctc | 918  |
| 20 | Ser | Thr | Arg | Ser | Val | Ser | Ala | Val | Thr              | Lys | Gly | Leu | Glu | Asn | Met | Leu |      |
|    |     |     | 280 |     |     |     |     | 285 |                  |     |     |     | 290 |     |     |     |      |
|    | aag | ttg | gga | gcc | agt | gtg | aac | atg | tac              | atg | ttc | cat | gga | ggt | acc | aac | 966  |
|    | Lys | Leu | Gly | Ala | Ser | Val | Asn | Met | Tyr              | Met | Phe | His | Gly | Gly | Thr | Asn |      |
|    |     | 295 |     |     |     |     | 300 |     |                  |     |     | 305 |     |     |     |     |      |
| 25 | ttt | gga | tat | tgg | aat | ggt | gcc | gat | aag              | aag | gga | cgc | ttc | ctt | ccg | att | 1014 |

|    | Phe | Gly | Tyr | Trp | Asn | Gly | Ala | Asp | Lys | Lys | Gly | Arg | Phe | Leu | Pro | Ile |      |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|    | 310 |     |     |     |     | 315 |     |     |     |     | 320 |     |     |     |     | 325 |      |
|    | act | acc | agc | tat | gac | tat | gat | gca | cct | ata | tct | gaa | gca | ggg | gac | ccc | 1062 |
|    | Thr | Thr | Ser | Tyr | Asp | Tyr | Asp | Ala | Pro | Ile | Ser | Glu | Ala | Gly | Asp | Pro |      |
| 5  |     |     |     |     | 330 |     |     |     |     | 335 |     |     |     |     | 340 |     |      |
|    | aca | cct | aag | ctt | ttt | gct | ctt | cga | gat | gtc | atc | agc | aag | ttc | cag | gaa | 1110 |
|    | Thr | Pro | Lys | Leu | Phe | Ala | Leu | Arg | Asp | Val | Ile | Ser | Lys | Phe | Gln | Glu |      |
|    |     |     |     | 345 |     |     |     |     | 350 |     |     |     |     | 355 |     |     |      |
|    | gtt | cct | ttg | gga | cct | tta | cct | ccc | ccg | agc | ccc | aag | atg | atg | ctt | gga | 1158 |
| 10 | ۷al | Pro | Leu | Gly | Pro | Leu | Pro | Pro | Pro | Ser | Pro | Lys | Met | Met | Leu | Gly |      |
|    |     |     | 360 |     |     |     |     | 365 |     |     |     |     | 370 |     |     |     |      |
|    | cct | gtg | act | ctg | cac | ctg | gtt | ggg | cat | tta | ctg | gct | ttc | cta | gac | ttg | 1206 |
|    | Pro | Val | Thr | Leu | His | Leu | Val | Gly | His | Leu | Leu | Ala | Phe | Leu | Asp | Leu | •    |
|    |     | 375 |     |     |     | •   | 380 |     |     |     |     | 385 |     |     |     |     |      |
| 15 | ctt | tgc | ccc | cgt | ggg | ccc | att | cat | tca | atc | ttg | cca | atg | acc | ttt | gag | 1254 |
|    | Leu | Cys | Pro | Arg | Gly | Pro | Ile | His | Ser | Ile | Leu | Pro | Met | Thr | Phe | Glu |      |
|    | 390 |     |     |     |     | 395 |     |     |     |     | 400 |     |     |     |     | 405 |      |
|    | gct | gţc | aag | cag | gac | cat | ggc | ttc | atg | ttg | tac | cga | acc | tat | atg | acc | 1302 |
|    | Ala | Val | Lys | Gln | Asp | His | Gly | Phe | Met | Leu | Tyr | Arg | Thr | Tyr | Met | Thr |      |
| 20 |     |     |     |     | 410 |     |     |     |     | 415 |     |     |     |     | 420 |     |      |
| •  |     |     | att |     |     |     |     |     |     |     |     |     |     |     |     |     | 1350 |
|    | His | Thr | Ile | Phe | Glu | Pro | Thr | Pro | Phe | Trp | Val | Pro | Asn | Asn | Gly | Val |      |
|    | •   |     |     | 425 |     |     |     |     | 430 |     |     |     |     | 435 |     |     |      |
|    |     |     | cgt |     |     |     |     |     |     | •   |     |     |     |     |     |     | 1398 |
| 25 | His | Asp | Arg | Ala | Tyr | Val | Met | Val | Asp | Gly | Val | Phe | Gln | Gly | Val | Val |      |

|    |     |     | 440 |     |     |     |     | 445 |     |     |     |     | 450 |     |     |       |      |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------|------|
|    | gag | cga | aat | atg | aga | gac | aaa | cta | ttt | ttg | acg | ggg | aaa | ctg | ggg | tcc   | 1446 |
|    | Glu | Arg | Asn | Met | Arg | Asp | Lys | Leu | Phe | Leu | Thr | Gly | Lys | Leu | Gly | Ser   |      |
|    |     | 455 |     |     |     |     | 460 |     |     |     |     | 465 |     |     |     |       |      |
| 5  | aaa | ctg | gat | atc | ttg | gtg | gag | aac | atg | ggg | agg | ctc | agc | ttt | ggg | tct   | 1494 |
|    | Lys | Leu | Asp | Ile | Leu | Val | Glu | Asn | Met | Gly | Arg | Leu | Ser | Phe | Gly | Ser   |      |
|    | 470 |     |     |     |     | 475 |     |     |     |     | 480 |     |     |     |     | 485   |      |
|    | aac | agc | agt | gac | ttc | aag | ggc | ctg | ttg | aag | cca | cca | att | ctg | ggg | caa   | 1542 |
|    | Asn | Ser | Ser | Asp | Phe | Lys | Gly | Leu | Leu | Lys | Pro | Pro | Ile | Leu | Gly | Gln   |      |
| 10 |     |     |     |     | 490 |     |     |     |     | 495 |     |     |     |     | 500 |       |      |
|    | aca | atc | ctt | acc | cag | tgg | atg | atg | ttc | cct | ctg | aaa | att | gat | aac | ctt   | 1590 |
|    | Thr | Ile | Leu | Thr | Gln | Trp | Met | Met | Phe | Pro | Leu | Lys | Ile | Asp | Asn | Leu   |      |
|    |     |     |     | 505 |     |     |     |     | 510 |     |     |     |     | 515 |     |       |      |
|    | gtg | aag | tgg | tgg | ttt | ccc | ctc | cag | ttg | cca | aaa | tgg | cca | tat | cct | caa   | 1638 |
| 15 | Val | Lys | Trp | Trp | Phe | Pro | Leu | Gln | Leu | Pro | Lys | Trp | Pro | Tyr | Pro | Gln   |      |
|    |     |     | 520 |     |     |     |     | 525 |     |     |     |     | 530 |     | •   |       |      |
|    | gct | cct | tct | ggc | ccc | aca | ttc | tac | tcc | aaa | aca | ttt | cca | att | tta | ggc   | 1686 |
|    | Ala | Pro | Ser | Gly | Pro | Thr | Phe | Tyr | Ser | Lys | Thr | Phe | Pro | Ile | Leu | Gly   |      |
|    |     | 535 |     |     |     |     | 540 |     |     |     |     | 545 |     |     |     |       |      |
| 20 | tca | gtt | ggg | gac | aca | ttt | cta | tat | cţa | cct | gga | tgg | acc | aag | ggc | caa . | 1734 |
|    | Ser | Val | Gly | Asp | Thr | Phe | Leu | Tyr | Leu | Pro | Gly | Trp | Thr | Lys | Gly | Gln   |      |
|    | 550 |     |     |     |     | 555 |     |     |     |     | 560 |     |     |     | ,   | 565   |      |
|    | gtc | tgg | atc | aat | ggg | ttt | aac | ttg | ggc | cgg | tac | tgg | aca | aag | cag | ggg   | 1782 |
|    | Val | Trp | Ile | Asn | Gly | Phe | Asn | Leu | Gly | Arg | Tyr | Trp | Thr | Ĺуs | Gln | Gly   |      |
| 25 |     |     |     |     | 570 |     |     |     |     | 575 |     |     |     |     | 580 |       |      |

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|    | cca  | caa   | cag   | acc  | ctc   | tac   | gtg   | cca   | aga   | ttc   | ctg  | ctg   | ttt   | cct   | agg   | gga    | 1830 |   |
|----|------|-------|-------|------|-------|-------|-------|-------|-------|-------|------|-------|-------|-------|-------|--------|------|---|
|    | Pro  | Gln   | Gln   | Thr  | Leu   | Tyr   | Val   | Pro   | Arg   | Phe   | Leu  | Leu   | Phe   | Pro   | Arg   | Gly    |      |   |
|    |      |       |       | 585  |       |       |       |       | 590   |       |      |       |       | 595   |       |        |      |   |
|    | gcc  | ctc   | aac   | aaa  | att   | aca   | ttg   | ctg   | gaa   | cta   | gaa  | gat   | gta   | cct   | ctc   | cag    | 1878 |   |
| 5  | Ala  | Leu   | Asn   | Lys  | Ile   | Thr   | Leu   | Leu   | Glu   | Leu   | Glu  | Asp   | Val   | Pro   | Leu   | Gln    |      |   |
|    |      |       | 600   |      |       |       |       | 605   |       |       |      |       | 610   |       |       |        |      |   |
|    | ccc  | caa   | gtc   | caa  | ttt   | ttg   | gat   | aag   | cct   | atc   | ctc  | aat   | agc   | act   | agt   | act    | 1926 |   |
|    | Pro  | Gln   | Val   | Gln  | Phe   | Leu   | Asp   | Lys   | Pro   | Ile   | Leu  | Asn   | Ser   | Thr   | Ser   | Thr    |      |   |
|    |      | 615   |       |      |       |       | 620   |       |       |       |      | 625   |       |       |       |        |      |   |
| 10 | ttg  | caċ   | agg   | aca  | cat   | atc   | aat   | tcc   | ctt   | tca   | gct  | gat   | aca   | ctg   | agt   | gcc    | 1974 | 0 |
|    | Leu  | His   | Arg   | Thr  | His   | Ile   | Asn   | Ser   | Leu   | Ser   | Ala  | Asp   | Thr   | Leu   | Ser   | Ala    |      | v |
| •  | 630  |       |       |      |       | 635   |       |       |       |       | 640  |       |       |       |       | 645    |      |   |
|    | tct  | gaa   | cca   | atg  | gag   | tta   | agt   | ggg   | cac   | tga   | aagg | gtago | icc č | ggc   | atggt | :g     | 2024 |   |
|    | Ser  | Glu   | Pro   | Met  | Glu   | Leu   | Ser   | Gly   | His   |       |      |       |       |       |       |        |      |   |
| L5 |      |       |       |      | 650   |       |       |       |       | 655   |      |       |       |       |       |        |      |   |
|    | gcto | atgo  | ct o  | taat | ccca  | ag ca | acttt | ggga  | a ggo | ctgag | gacg | ggto  | gatt  | cac   | ctgag | ggtcag | 2084 |   |
|    | gact | tcaa  | iga d | cago | ctg   | jc ca | acat  | ggtg  | j aaa | accc  | gtc  | tcca  | ctaa  | aaa a | ataca | aaaat  | 2144 |   |
|    | tago | cggg  | gcg t | gato | gtgg  | gg ca | accto | ctaat | ccc   | cagct | act  | tggg  | gaggo | etg a | agggo | aggag  | 2204 |   |
|    | aatt | gctt  | ga a  | tcca | aggag | g ca  | gago  | jttgo | agt   | gagt  | gga  | ggtt  | gtac  | cca ( | ctgca | ectcca | 2264 |   |
| 20 | gcct | .ggct | ga c  | agto | gagad | a ct  | ccat  | ctca  | aaa   | aaaa  | aaaa | aaaa  | aaaa  | aaa a | aagta | accct  | 2324 |   |
|    | tgga | eccto | igg a | cato | gagt  | g gg  | gcago | gatco | ctt   | ggto  | jctg | gcca  | acggt | ga (  | cccta | aggaa  | 2384 |   |
|    | ctaa | aggo  | ca c  | agto | ccto  | et ga | atgt  | aagt  | aca   | agta  | ıcac | atto  | ctto  | jcc ( | aaact | ttatt  | 2444 |   |
|    | gtga | ttaa  | aa t  | tcca | agaga | ac ag | ŗt    |       |       |       |      |       |       |       |       |        | 2467 |   |

25 <210> 84

189/346

<211> 1450

<212> DNA

<213> Homo sapiens

5 <220>

<221> CDS

<222> (245)..(1417)

<400> 84

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15 Met Gly Met Asp Asp Cys Asp Ser Phe Phe Pro Gly Pro Leu Val

1 5 10 15

gct att att tgt gac ata ctt gga gag aaa act acc tcc att ctt ggg 337
Ala Ile Ile Cys Asp Ile Leu Gly Glu Lys Thr Thr Ser Ile Leu Gly

20 25 30

20 gct ttt gtt gtt act ggt gga tat ctg atc agc agc tgg gcc aca agt 385
Ala Phe Val Val Thr Gly Gly Tyr Leu Ile Ser Ser Trp Ala Thr Ser

35 40 45

att cct ttt ctt tgt gtg act atg gga ctt cta ccc ggt ttg ggt tct 433

Ile Pro Phe Leu Cys Val Thr Met Gly Leu Leu Pro Gly Leu Gly Ser

25 50 55 60

|    | gct | ttc | tta | tac | caa | gtg | gct | gct | gtg | gta | act | acc | aaa | tac | ttc | aaa | 481 |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Ala | Phe | Leu | Tyr | Gln | Val | Ala | Ala | Val | Val | Thr | Thr | Lys | Tyr | Phe | Lys |     |
|    |     | 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     |     |
|    | aaa | cga | ttg | gct | ctt | tct | aca | gct | att | gcc | cgt | tct | ggg | atg | gga | ctg | 529 |
| 5  | Lys | Arg | Leu | Ala | Leu | Ser | Thr | Ala | Ile | Ala | Arg | Ser | Gly | Met | Gly | Leu |     |
|    | 80  |     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
|    | act | ttt | ctt | ttg | gca | ccc | ttt | aca | aaa | ttc | ctg | ata | gat | ctg | tat | gac | 577 |
|    | Thr | Phe | Leu | Leu | Ala | Pro | Phe | Thr | Lys | Phe | Leu | Ile | Asp | Leu | Tyr | Asp |     |
|    |     |     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
| 10 | tgg | aca | gga | gcc | ctt | ata | tta | ttt | gga | gct | atc | gca | ttg | aat | ttg | gtg | 625 |
|    | Trp | Thr | Gly | Ala | Leu | Ile | Leu | Phe | Gly | Ala | Ile | Ala | Leu | Asn | Leu | Val |     |
|    |     |     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
|    | cct | tct | agt | atg | ctc | tta | aga | ccc | atc | cat | atc | aaa | agt | gag | aac | aat | 673 |
|    | Pro | Ser | Ser | Met | Leu | Leu | Arg | Pro | Ile | His | Ile | Lys | Ser | Glu | Asn | Asn |     |
| 15 |     |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     | •   |     |
|    | tct | ggt | att | aaa | gat | aaa | ggc | agc | agt | ttg | tct | gca | cat | ggt | cca | gag | 721 |
|    | Ser | Gly | Ile | Lys | Asp | Lys | Gly | Ser | Ser | Leu | Ser | Ala | His | Gly | Pro | Glu |     |
|    |     | 145 |     |     |     |     | 150 |     | •   |     |     | 155 |     |     |     |     |     |
|    | gca | cat | gca | aca | gaa | aca | Cac | tgc | cat | gag | aca | gaa | gag | tct | acc | atc | 769 |
| 20 | Ala | His | Ala | Thr | Glu | Thr | His | Cys | His | Glu | Thr | Glu | Glu | Ser | Thr | Ile |     |
|    | 160 |     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
|    | aag | gac | agt | act | acg | cag | aag | gct | gga | cta | cct | agc | aaa | aat | tta | aca | 817 |
|    | Lys | Asp | Ser | Thr | Thr | Gln | Lys | Ala | Gly | Leu | Pro | Ser | Lys | Asn | Leu | Thr |     |
|    |     |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
| 25 | gtc | tca | caa | aat | caa | agt | gaa | gag | ttc | tac | aat | ggg | cct | aac | agg | aac | 865 |

|    | Val | Ser | Gln | Asn | Gln | Ser | Glu | Glu | Phe | Tyr | Asn | Gly | Pro | Asn | Arg | Asn |      |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|    |     |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |      |
|    | aga | ctg | tta | tta | aag | agt | gat | gaa | gaa | agt | gat | aag | gtt | att | tcg | tgg | 913  |
|    | Arg | Leu | Leu | Leu | Lys | Ser | Asp | Glu | Glu | Ser | Asp | Lys | Val | Ile | Ser | Trp |      |
| 5  |     |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |      |
|    | agc | tgc | aaa | caa | ctg | ttt | gac | att | tct | ctc | ttt | aga | aat | cct | ttc | ttc | 961  |
|    | Ser | Cys | Lys | Gln | Leu | Phe | Asp | Ile | Ser | Leu | Phe | Arg | Asn | Pro | Phe | Phe |      |
|    |     | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     |      |
|    | tac | ata | ttt | act | tgg | tct | ttt | ctc | ctc | agt | cag | tta | gca | tac | ttc | atc | 1009 |
| 10 | Tyr | Ile | Phe | Thr | Trp | Ser | Phe | Leu | Leu | Ser | Gln | Leu | Ala | Tyr | Phe | Ile |      |
|    | 240 |     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |      |
|    | cct | acc | ttt | cac | ctg | gta | gcc | aga | gcc | aaa | aca | ctg | ggg | att | gac | atc | 1057 |
|    | Pro | Thr | Phe | His | Leu | Val | Ala | Arg | Ala | Lys | Thr | Leu | Gly | Ile | Asp | Ile |      |
|    |     |     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |      |
| 15 | atg | gat | gcc | tct | tac | ctt | gtt | tct | gta | gca | ggt | atc | ctt | gag | acg | gtc | 1105 |
|    | Met | Asp | Ala | Ser | Tyr | Leu | Val | Ser | Val | Ala | Gly | Ile | Leu | Glu | Thr | Val |      |
|    |     |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |      |
|    | agt | cag | att | att | tct | gga | tgg | gtt | gct | gat | caa | aac | tgg | att | aag | aag | 1153 |
|    | Ser | Gln | Ile | Ile | Ser | Gly | Trp | Val | Ala | Asp | Gln | Asn | Trp | Ile | Lys | Lys |      |
| 20 |     |     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |      |
|    | taț | cat | tac | cac | aag | tct | tac | ctc | atc | ctc | tgc | ggc | atc | act | aac | ctg | 1201 |
|    | Tyr | His | Tyr | His | Lys | Ser | Tyr | Leu | Ile | Leu | Cys | Gly | Ile | Thr | Asn | Leu |      |
|    |     | 305 |     |     |     |     | 310 |     | •   |     |     | 315 |     |     |     |     |      |
|    | ctt | gct | cct | tta | gcc | acc | aca | ttt | cca | cta | ctt | atg | acc | tac | acc | atc | 1249 |
| 25 | Leu | Ala | Pro | Leu | Ala | Thr | Thr | Phe | Pro | Leu | Leu | Met | Thr | Tyr | Thr | Ile |      |

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320 325 330 335 tgc ttt gcc atc ttt gct ggt ggt tac ctg gca ttg ata ctg cct gta 1297 Cys Phe Ala Ile Phe Ala Gly Gly Tyr Leu Ala Leu Ile Leu Pro Val 340 345 350 5 ctg gtt gat ctg tgt agg aat tct aca gta aac agg ttt ttg gga ctt 1345 Leu Val Asp Leu Cys Arg Asn Ser Thr Val Asn Arg Phe Leu Gly Leu 355 360 365 gcc agt ttc ttt gct ggg atg gct gtc ctt tct gga cca cct ata gca Ala Ser Phe Phe Ala Gly Met Ala Val Leu Ser Gly Pro Pro Ile Ala 10 370 375 380 ggt aac acc ttc acc aca ttc tga acaaatttca atagcaataa aagagaaaaa 1447 Gly Asn Thr Phe Thr Thr Phe 385 390 ctg 1450 15 <210> 85 <211> 1897 <212> DNA <213> Homo sapiens 20 <220> <221> CDS <222> (8)..(1366)

25

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|----|------|------|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|-------|----------|-----|-----|
|    |      |      | Met | Glu | Leu | Ala | Leu | Arg  | Arg | Ser | Pro | Val | Pro | Arg   | Trp      | Leu |     |
|    |      |      | 1   |     |     |     | 5   |      |     |     |     | 10  |     |       |          |     |     |
|    | ctg  | ctg  | ctg | ccg | ctg | ctg | ctg | ggc  | ctg | aac | gca | gga | gct | gtc   | att      | gac | 97  |
| 5  | Leu  | Leu  | Leu | Pro | Leu | Leu | Leu | Gly  | Leu | Asn | Ala | Gly | Ala | Val   | Ile      | Asp |     |
|    | 15   |      |     |     |     | 20  |     |      |     |     | 25  |     |     |       |          | 30  |     |
|    | tgg  | ccc  | aca | gag | gag | ggc | aag | gaa  | gta | tgg | gat | tat | gtg | acg   | gtc      | cgc | 145 |
|    | Trp  | Pro  | Thr | Glu | Glu | Gly | Lys | Glu  | Val | Trp | Asp | Tyr | Val | Thr   | Val      | Arg |     |
|    |      |      |     |     | 35  |     |     |      |     | 40  |     |     |     |       | 45       |     |     |
| 10 | aag  | gat  | gcc | tac | atg | ttc | tgg | tgg  | ctc | tat | tat | gcc | acc | aac   | tcc      | tgc | 193 |
|    | Lys  | Asp  | Ala | Tyr | Met | Phe | Trp | Trp  | Leu | Tyr | Tyr | Ala | Thr | Asn   | Ser      | Cys |     |
|    |      |      |     | 50  |     |     |     |      | 55  |     |     |     | ,   | 60    |          |     |     |
|    | aag  | aac  | ttc | tca | gaa | ctg | ccc | ctg  | gtc | atg | tgg | ctt | cag | ggc   | ggt      | cca | 241 |
|    | Lys  | Asn  | Phe | Ser | Glu | Leu | Pro | Leu  | Val | Met | Trp | Leu | Gln | Gly   | Gly      | Pro |     |
| 15 |      |      | 65  |     |     |     |     | 70   |     |     |     |     | 75  |       |          |     |     |
|    | ggc  | ggt  | tct | agc | act | gga | ttt | gga  | aac | ttt | gag | gaa | att | ggg   | ccc      | ctt | 289 |
|    | Gly  | Gly  | Ser | Ser | Thr | Gly | Phe | Gly  | Asn | Phe | Glu | Glu | Ile | Gly   | Pro      | Leu |     |
|    |      | 80   |     |     |     |     | 85  |      |     |     |     | 90  |     |       |          |     |     |
|    | gac  | agt  | gat | ctc | aaa | cca | cgg | aaa  | acc | acc | tgg | ctc | cag | gct   | gcc      | agt | 337 |
| 20 | Asp  | Ser  | Asp | Leu | Lys | Pro | Arg | Lys  | Thr | Thr | Trp | Leu | Gln | Ala   | Ala      | Ser |     |
|    | 95   |      |     |     |     | 100 | •   |      |     |     | 105 |     |     |       |          | 110 |     |
|    | ctc  | cta  | ttt | gtg | gat | aat | ccc | gtg  | agc | act | aga | ttc | agt | tat   | ata      | aat | 385 |
|    |      |      | Phe |     |     |     |     |      |     |     |     |     | _   |       |          |     |     |
|    |      |      |     |     | 115 |     |     |      |     | 120 | 2   |     |     | - 4 - | 125      |     |     |
| 25 | aat  | aat  | ggt | acc |     | acc | 220 | usc. | cta |     | 2+~ | ata | act | tca   |          | ato | 422 |
|    | 220  | ~gc  | 990 | 900 | Cuc | guu | aay | gac  | cug | gul | aly | grg | gut | LUA   | yac      | acy | 433 |

|    | Gly | Ser | Gly | Ala | Tyr | Ala | Lys | Asp | Leu | Ala | Met | Val | Ala | Ser | Asp | Met |     |            |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------------|
|    |     |     |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |            |
|    | atg | gtt | ctc | ctg | aag | acc | ttc | ttc | agt | tgc | cac | aaa | gaa | ttc | cag | aca | 481 |            |
|    | Met | Val | Leu | Leu | Lys | Thr | Phe | Phe | Ser | Суѕ | His | Lys | Glu | Phe | Gln | Thr |     |            |
| 5  |     |     | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     |            |
|    | gtt | cca | ttc | tac | att | ttc | tca | gag | tcc | tat | gga | gga | aaa | atg | gca | gct | 529 |            |
|    | Val | Pro | Phe | Tyr | Ile | Phe | Ser | Glu | Ser | Tyr | Gly | Gly | Lys | Met | Ala | Ala |     |            |
|    |     | 160 |     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     |     |            |
|    | ggc | att | ggt | cta | gag | ctt | tat | aag | gcc | att | cag | cga | ggg | acc | atc | aag | 577 |            |
| 10 | Gly | Ile | Gly | Leu | Glu | Leu | Tyr | Lys | Ala | Ile | Gln | Arg | Gly | Thr | Ile | Lys |     | · <b>.</b> |
|    | 175 |     |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |            |
|    | tgc | aac | ttt | gcg | ggg | gtt | gcc | ttg | ggt | gat | tcc | tgg | atc | tcc | cct | gtt | 625 |            |
|    | Cys | Asn | Phe | Ala | Gly | Val | Ala | Leu | Gly | Asp | Ser | Trp | Ile | Ser | Pro | Val |     |            |
|    |     |     |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |            |
| 15 | gat | tcg | gtg | ctc | tcc | tgg | gga | cct | tac | ctg | tac | agc | atg | tct | ctt | ctc | 673 |            |
|    | Asp | Ser | Val | Leu | Ser | Trp | Gly | Pro | Tyr | Leu | Tyr | Ser | Met | Ser | Leu | Leu |     |            |
|    |     |     |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |            |
|    | gaa | gac | aaa | ggt | ctg | gca | gag | gtg | tct | aag | gtt | gca | gag | caa | gta | ctg | 721 |            |
|    | Glu | Asp | Lys | Gly | Leu | Ala | Glu | Val | Ser | Lys | Val | Ala | Glu | Gln | Val | Leu |     |            |
| 20 |     |     | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     |            |
|    | aat | gcc | gta | aat | aag | ggg | ctc | tac | aga | gag | gcc | aca | gag | ctg | tgg | ggg | 769 |            |
|    | Asn | Ala | Val | Asn | Lys | Gly | Leu | Tyr | Arg | Glu | Ala | Thr | Glu | Leu | Trp | Gly |     |            |
|    |     | 240 |     |     |     |     | 245 |     |     |     |     | 250 |     | •   |     |     |     |            |
|    | aaa | gca | gaa | atg | atc | att | gaa | cag | aac | aca | gat | ggg | gtg | aac | ttc | tat | 817 |            |
| 25 | Lys | Ala | Glu | Met | Ile | Ile | Glu | Gln | Asn | Thr | Asp | Gly | Val | Asn | Phe | Tyr |     |            |

|    | 255 |     |     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |      |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|    | aac | atc | tta | act | aaa | agc | act | ccc | acg | tct | aca | atg | gag | tcg | agt | cta | 865  |
|    | Asn | Ile | Leu | Thr | Lys | Ser | Thr | Pro | Thr | Ser | Thr | Met | Glu | Ser | Ser | Leu |      |
|    |     |     |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |      |
| 5  | gaa | ttc | aca | cag | agc | cac | cta | gtt | tgt | ctt | tgt | cag | cgc | cac | gtg | aga | 913  |
|    | Glu | Phe | Thr | Gln | Ser | His | Leu | Val | Cys | Leu | Cys | Gln | Arg | His | Val | Arg |      |
|    |     |     |     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |      |
|    | cac | cta | caa | cga | gat | gcc | tta | agc | cag | ctc | atg | aat | ggc | ccc | atc | aga | 961  |
|    | His | Leu | Gln | Arg | Asp | Ala | Leu | Ser | Gln | Leu | Met | Asn | Gly | Pro | Ile | Arg |      |
| 10 |     |     | 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |      |
|    | aag | aag | ctc | aaa | att | att | cct | gag | gat | caa | tcc | tgg | gga | ggc | cag | gct | 1009 |
|    | Lys | Lys | Leu | Lys | Ile | Ile | Pro | Glu | Asp | Gln | Ser | Trp | Gly | Gly | Gln | Ala |      |
|    |     | 320 |     |     |     |     | 325 |     |     |     |     | 330 |     |     |     |     |      |
|    | acc | aac | gtc | ttt | gtg | aac | atg | gag | gag | gac | ttc | atg | aag | cca | gtc | att | 1057 |
| 15 | Thr | Asn | Val | Phe | Val | Asn | Met | Glu | Glu | Asp | Phe | Met | Lys | Pro | Val | Ile |      |
|    | 335 |     |     |     |     | 340 |     |     |     |     | 345 |     |     |     |     | 350 |      |
|    | agc | att | gtg | gac | gag | ttg | ctg | gag | gca | ggg | atc | aac | gtg | acg | gtg | tat | 1105 |
|    | Ser | Ile | Val | Asp | Glu | Leu | Leu | Glu | Ala | Gly | Ile | Asn | Val | Thr | Val | Tyr |      |
|    |     |     |     |     | 355 |     |     |     |     | 360 |     |     |     |     | 365 |     |      |
| 20 | aat | gga | cag | ctg | gat | ctc | atc | gta | gat | acc | atg | ggt | cag | gag | gcc | tgg | 1153 |
|    | Asn | Gly | Gln | Leu | Asp | Leu | Ile | Val | Asp | Thr | Met | Gly | Gln | Glu | Ala | Trp |      |
|    |     |     |     | 370 |     |     |     |     | 375 |     |     |     |     | 380 |     |     |      |
|    | gtg | cgg | aaa | ctg | aag | tgģ | cca | gaa | ctg | cct | aaa | ttc | agt | cag | ctg | aag | 1201 |
|    | Val | Arg | Lys | Leu | Lys | Trp | Pro | Glu | Leu | Pro | Lys | Phe | Ser | Gln | Leu | Lys |      |
| 25 |     |     | 385 |     |     |     |     | 390 |     |     |     |     | 395 |     |     |     |      |

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|    | tgg  | aag      | gcc   | ctg   | tac   | agt   | gac   | cct  | aaa   | tct   | ctg  | gaa   | aca   | tct   | gct   | ttt    | 1249 |
|----|------|----------|-------|-------|-------|-------|-------|------|-------|-------|------|-------|-------|-------|-------|--------|------|
|    | Trp  | Lys      | Ala   | Leu   | Tyr   | Ser   | Asp   | Pro  | Lys   | Ser   | Leu  | Glu   | Thr   | Ser   | Ala   | Phe    |      |
|    |      | 400      |       |       |       |       | 405   |      |       |       |      | 410   |       |       | •     |        |      |
|    | gtc  | aag      | tcc   | tac   | aag   | aac   | ctt   | gct  | ttc   | tac   | tgg  | att   | ctg   | aaa   | gct   | ggt    | 1297 |
| 5  | Val  | Lys      | Ser   | Tyr   | Lys   | Asn   | Leu   | Ala  | Phe   | Tyr   | Trp  | Ile   | Leu   | Lys   | Ala   | Gly    |      |
|    | 415  |          |       |       |       | 420   |       |      |       |       | 425  |       |       |       |       | 430    |      |
|    | cat  | atg      | gtt   | cct   | tct   | gac   | caa   | ggg  | gac   | atg   | gct  | ctg   | aag   | atg   | atg   | aga    | 1345 |
|    | His  | Met      | Val   | Pro   | Ser   | Asp   | Gln   | Gly  | Asp   | Met   | Ala  | Leu   | Lys   | Met   | Met   | Arg    |      |
|    |      |          |       |       | 435   |       |       |      |       | 440   |      |       |       |       | 445   |        |      |
| 10 | ctg  | gtg      | act   | cag   | caa   | gaa   | ţag   | gate | ggato | ggg g | gctg | gagat | tg ag | gctg  | gttt  | J      | 1396 |
|    | Leu  | ۷al      | Thr   | Gln   | Gln   | Glu   |       |      |       |       |      |       |       |       |       |        |      |
|    |      |          |       | 450   |       |       |       |      |       |       |      |       |       |       |       |        |      |
|    | gcct | tgg      | ggc a | acaga | agcto | ga go | ctgag | ggcc | g cto | gaago | ctgt | agga  | aagc  | gcc a | attci | ttccct | 1456 |
|    |      |          |       |       |       |       |       |      |       | •     |      |       |       |       |       | aatca  |      |
| 15 |      |          |       |       | •     |       |       |      |       |       |      |       |       |       |       | tttta  |      |
|    |      |          |       |       |       |       |       |      |       |       |      |       |       |       | _     | ttatga |      |
|    |      |          |       | _     | _     |       |       |      | _     |       |      | _     |       |       |       | gtaaat |      |
|    |      |          |       |       |       |       |       |      |       |       |      |       |       |       |       | gtcctt |      |
|    |      |          |       |       |       |       |       |      |       |       |      |       |       |       |       | actcta |      |
| 20 |      |          |       |       |       |       |       |      |       |       |      |       |       |       |       | caataa |      |
| 20 |      |          |       |       |       |       | acat  | accd | y La  | Late  | Lyaa | aca   |       |       | acyc  | -aalad |      |
|    | acy  | المانانا | tct   | uldā  | اعددا | LL C  |       |      |       |       |      |       |       |       |       |        | 1897 |

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197/346

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Met Arg Pro Ala

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ttc gcc ctg tgc ctc ctc tgg cag gcg ctc tgg ccc ggg ccg ggc ggc 102
Phe Ala Leu Cys Leu Leu Trp Gln Ala Leu Trp Pro Gly Pro Gly Gly

5 10 15 20

ggc gaa cac ccc act gcc gac cgt gct ggc tgc tcg gcc tcg ggg gcc 150

Gly Glu His Pro Thr Ala Asp Arg Ala Gly Cys Ser Ala Ser Gly Ala

tgc tac agc ctg cac cac gct acc atg aag cgg cag gcg gcc gag gag 198 Cys Tyr Ser Leu His His Ala Thr Met Lys Arg Gln Ala Ala Glu Glu

30

35

40 45 50

20 gcc tgc atc ctg cga ggt ggg gcg ctc agc acc gtg cgt gcg ggc gcc 246
Ala Cys Ile Leu Arg Gly Gly Ala Leu Ser Thr Val Arg Ala Gly Ala

55 60 65

gag ctg cgc gct gtg ctc gcg ctc ctg cgg gca ggc cca ggg ccc gga 294 Glu Leu Arg Ala Val Leu Ala Leu Leu Arg Ala Gly Pro Gly Pro Gly

25 70 75 80

|    | ggg | ggc | tcc | aaa | gac | ctg | ctg  | ttc | tgg | gtc | gca | ctg | gag | cgc | agg | cgt | 342 |
|----|-----|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Gly | Gly | Ser | Lys | Asp | Leu | Leu  | Phe | Trp | Val | Ala | Leu | Glu | Arg | Arg | Arg |     |
|    | 85  |     |     |     |     | 90  |      |     |     | Ī   | 95  |     |     |     |     | 100 |     |
|    | tcc | cac | tgc | acc | ctg | gag | aac  | gag | cct | ttg | cgg | ggt | ttc | tcc | tgg | ctg | 390 |
| 5  | Ser | His | Cys | Thr | Leu | Glu | Asn  | Glu | Pro | Leu | Arg | Gly | Phe | Ser | Trp | Leu |     |
|    |     |     |     |     | 105 |     |      |     |     | 110 |     |     |     |     | 115 |     |     |
|    | tcc | tcc | gac | ccc | ggc | ggt | ctc  | gaa | agc | gac | acg | ctg | cag | tgg | gtg | gag | 438 |
|    | Ser | Ser | Asp | Pro | Gly | Gly | Leu  | Glu | Ser | Asp | Thr | Leu | Gln | Trp | Val | Glu |     |
|    |     |     |     | 120 |     |     |      |     | 125 |     |     |     |     | 130 |     |     |     |
| 10 | gag | ccc | caa | cgc | tcc | tgc | acc  | gcg | cgg | aga | tgc | gcg | gta | ctc | cag | gcc | 486 |
|    | Glu | Pro | Gln | Arg | Ser | Cys | Thr  | Ala | Arg | Arg | Cys | Ala | Val | Leu | Gln | Ala |     |
|    |     |     | 135 |     |     |     |      | 140 |     |     |     |     | 145 |     |     |     |     |
|    | acc | ggt | ggg | gtc | gag | ccc | gca  | ggc | tgg | aag | gag | atg | cga | tgc | cac | ctg | 534 |
|    | Thr | Gly | Gly | Val | Glu | Pro | Ala  | Gly | Trp | Lys | Glu | Met | Arg | Cys | His | Leu |     |
| 15 |     | 150 |     |     |     |     | 155  |     |     |     |     | 160 |     |     |     | ٠   |     |
|    | cgc | gcc | aac | ggc | tac | ctg | tgc  | aag | tac | cag | ttt | gag | gtc | ttg | tgt | cct | 582 |
|    | Arg | Ala | Asn | Gly | Tyr | Leu | Cys  | Lys | Tyr | Gln | Phe | Glu | Val | Leu | Суз | Pro |     |
|    | 165 |     |     |     |     | 170 |      |     |     |     | 175 |     |     |     |     | 180 |     |
|    | gcg | ccg | cgc | CCC | ggg | gcc | gʻcc | tct | aac | ttg | agc | tat | cgc | gcg | ccc | ttc | 630 |
| 20 | Ala | Pro | Arg | Pro | Gly | Ala | Ala  | Ser | Asn | Leu | Ser | Tyr | Arg | Ala | Pro | Phe |     |
|    |     |     |     |     | 185 |     |      |     |     | 190 |     |     |     |     | 195 |     |     |
|    | cag | ctg | cac | agc | gcc | gct | ctg  | gac | ttc | agt | cca | cct | ggg | acc | gag | gtg | 678 |
|    | Gln | Leu | His | Ser | Ala | Ala | Leu  | Asp | Phe | Ser | Pro | Pro | Gly | Thr | Glu | Val |     |
|    |     |     |     | 200 |     |     |      |     | 205 |     |     |     |     | 210 |     |     |     |
| 25 | agt | gcg | ctc | tgc | cgg | qqa | caq  | ctc | cca | atc | tca | att | act | tac | atc | aca | 726 |

|    | Ser | Ala | Leu | Cys | Arg | Gly | Gln | Leu | Pro | Ile | Ser | Val | Thr | Cys | Ile | Ala |      |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|    |     |     | 215 |     |     |     |     | 220 |     |     |     |     | 225 |     |     |     |      |
|    | gac | gaa | atc | ggc | gct | cgc | tgg | gac | aaa | ctc | tcg | ggc | gat | gtg | ttg | tgt | 774  |
|    | Asp | Glu | Ile | Gly | Ala | Arg | Trp | Asp | Lys | Leu | Ser | Gly | Asp | Val | Leu | Cys |      |
| 5  |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |     |     |     |     |      |
|    | ccc | tgc | ccc | gġg | agg | tac | ctc | cgt | gct | ggc | aaa | tgc | gca | gag | ctc | cct | 822  |
|    | Pro | Cys | Pro | Gly | Arg | Tyr | Leu | Arg | Ala | Gly | Lys | Cys | Ala | Glu | Leu | Pro |      |
|    | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |     |     |     | 260 |      |
|    | aac | tgc | cta | gac | gac | ttg | gga | ggc | ttt | gcc | tgc | gaa | tgt | gct | acg | ggc | 870  |
| 10 | Asn | Cys | Leu | Asp | Asp | Leu | Gly | Gly | Phe | Ala | Cys | Glu | Cys | Ala | Thr | Gly |      |
|    |     |     |     |     | 265 |     |     |     |     | 270 |     |     |     |     | 275 |     |      |
|    | ttc | gag | ctg | ggg | aag | gac | ggc | cgc | tct | tgt | gtg | acc | agt | ggg | gaa | gga | 918  |
| •  | Phe | Glu | Leu | Gly | Lys | Asp | Gly | Arg | Ser | Cys | Val | Thr | Ser | Gly | Glu | Gly |      |
|    |     |     |     | 280 |     |     |     |     | 285 |     |     |     |     | 290 |     |     |      |
| 15 | cag | ccg | acc | ctt | ggg | ggg | acc | ggg | gtg | ccc | acc | agg | cgc | ccg | ccg | gcc | 966  |
|    | Gln | Pro | Thr | Leu | Gly | Gly | Thr | Gly | Val | Pro | Thr | Arg | Arg | Pro | Pro | Ala |      |
|    |     |     | 295 |     |     |     |     | 300 |     |     |     |     | 305 |     |     |     |      |
|    | act | gca | acc | agc | ccc | gtg | ccg | cag | aga | aca | tgg | cca | atc | agg | gtc | gac | 1014 |
|    | Thr | Ala | Thr | Ser | Pro | Val | Pro | Gln | Arg | Thr | Trp | Pro | Ile | Arg | Val | Asp |      |
| 20 |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |     |     |     |     |      |
|    | gag | aag | ctg | gga | gag | aca | cca | ctt | gtc | cct | gaa | caa | gac | aat | tca | gta | 1062 |
|    | Glu | Lys | Leu | Gly | Glu | Thr | Pro | Leu | Val | Pro | Glu | Gln | Asp | Asn | Ser | Val |      |
|    | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |     |     |     | 340 |      |
|    | aca | tct | att | cct | gag | att | cct | cga | tgg | gga | tca | cag | agc | acg | atg | tct | 1110 |
| 25 | Thr | Ser | Ile | Pro | Glu | Ile | Pro | Arg | Trp | Gly | Ser | Gln | Ser | Thr | Met | Ser |      |

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|    |      |     |     |     | 345 |     |     |     |     | 350 |     |          |     |     | 355 |     |      |
|----|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|----------|-----|-----|-----|-----|------|
|    | acc  | ctt | caa | atg | tcc | ctt | caa | gcc | gag | tca | aag | gcc      | act | atc | acc | cca | 1158 |
|    | Thr  | Leu | Gln | Met | Ser | Leu | Gln | Ala | Glu | Ser | Lys | Ala      | Thr | Ile | Thr | Pro |      |
|    |      |     |     | 360 |     |     |     |     | 365 |     |     |          |     | 370 |     |     |      |
| 5  | tca  | ggg | agc | gtg | att | tcc | aag | ttt | aat | tct | acg | act      | tcc | tct | gcc | act | 1206 |
|    | Ser  | Gly | Ser | Val | Ile | Ser | Lys | Phe | Asn | Ser | Thr | Thr      | Ser | Ser | Ala | Thr |      |
|    |      |     | 375 |     |     |     |     | 380 |     |     |     |          | 385 |     |     |     |      |
|    | cct  | cag | gct | ttc | gac | tcc | tcc | tct | gcc | gtg | gtc | ttc      | ata | ttt | gtg | agc | 1254 |
|    | Pro  | Gln | Ala | Phe | Asp | Ser | Ser | Ser | Ala | Val | Val | Phe      | Ile | Phe | Val | Ser |      |
| 10 |      | 390 |     |     |     |     | 395 |     |     |     |     | 400      |     |     |     |     |      |
|    | aca  | gca | gta | gta | gtg | ttg | gtg | atc | ttg | acc | atg | aca      | gta | ctg | ggg | ctt | 1302 |
|    | Thr  | Ala | Val | Val | Val | Leu | Val | Ile | Leu | Thr | Met | Thr      | Val | Leu | Gly | Leu |      |
|    | 405  |     |     |     |     | 410 |     |     |     |     | 415 |          |     |     |     | 420 |      |
|    | .gtc | aag | ctc | tgc | ttt | cac | gaa | agc | ccc | tct | tcc | cag      | cca | agg | aag | gag | 1350 |
| 15 | Val  | Lys | Leu | Cys | Phe | His | Glu | Ser | Pro | Ser | Ser | Gln      | Pro | Arg | Lys | Glu |      |
|    |      |     |     |     | 425 |     |     |     |     | 430 |     |          |     |     | 435 |     |      |
|    | tct  | atg | ggc | ccg | ccg | ggc | ctg | gag | agt | gat | cct | gag<br>= | ccc | gct | gct | ttg | 1398 |
|    | Ser  | Met | Gly | Pro | Pro | Gly | Leu | Glu | Ser | Asp | Pro | Glu      | Pro | Ala | Ala | Leu |      |
|    |      |     |     | 440 |     |     |     |     | 445 |     |     |          |     | 450 |     |     |      |
| 20 | ggc  | tcc | agt | tct | gca | cat | tgc | aca | aac | aat | ggg | gtg      | aaa | gtc | ggg | gac | 1446 |
|    | Gly  | Ser | Ser | Ser | Ala | His | Cys | Thr | Asn | Asn | Gly | Val      | Lys | Val | Gly | Asp |      |
|    |      |     | 455 |     |     |     |     | 460 |     |     |     |          | 465 |     |     |     |      |
|    | tgt  | gat | ctg | cgg | gac | aga | gca | gag | ggt | gcc | ttg | ctg      | gcg | gag | tcc | cct | 1494 |
|    | Суз  | Asp | Leu | Arg | Asp | Arg | Ala | Glu | Gly | Ala | Leu | Leu      | Ala | Glu | Ser | Pro |      |
| 25 |      | 470 |     |     |     |     | 475 |     |     |     |     | 480      |     |     |     |     |      |

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ctt ggc tct agt gat gca tag ggaaacaggg gacatgggca ctcctgtgaa 1545 Leu Gly Ser Ser Asp Ala 485 490 cagtttttca cttttgatga aacggggaac caagaggaac ttacttgtgt aactgacaat 1605 5 ttctgcagaa atcccccttc ctctaaattc cctttactcc actgaggagc taaatcagaa 1665 ctgcacactc cttccctgat gatagaggaa gtggaagtgc ctttaggatg gtgatactqg 1725 gggaccgggt agtgctgggg agagatattt tcttatgttt attcggagaa tttggagaag 1785 tgattgaact tttcaagaca ttggaaacaa atagaacaca atataattta cattaaaaaa 1845 taatttctac c 1856 . 10 <210> 87 <211> 2173 <212> DNA <213> Homo sapiens 15 <220> <221> CDS <222> (262)..(1440) 20 <400> 87 gtttggagtt gtcaccactt tcccctctcc gtctcctgcg ggcgcaatgg aggaggagga 60 tgaqgaagcg cgggcgctcc tggcaggcgg ccctgacgag gccgacagag gtgccccggc 120 cgcccctgga gccctgccgg ccctctgcga ccccagtcgc ctggcgcacc ggcttttggt 180 gctgttactg atgtgcttcc ttggctttgc tatttttgct atgataatcc tgctgccctt 240

cagactcaag ttaaacgaga t atg caa gtg aat acc acg aaa ttc atg ctg 291

25

| Į.    | Leu | Met | Phe | Lys | Thr | Thr | Asn | Val | Gln | Met |     |     |     |     |     |     |     |
|-------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|       | 10  |     |     |     |     | 5   |     |     |     | 1   |     |     |     |     |     |     |     |
| . 339 | ggt | ttt | ttc | tgt | ttg | gtt | gta | aat | ccc | tgg | tct | tat | tgg | gcc | tat | ctg |     |
| ,     | Gly | Phe | Phe | Cys | Leu | Val | Val | Asn | Pro | Trp | Ser | Tyr | Trp | Ala | Tyr | Leu |     |
|       |     | 25  |     |     |     |     | 20  |     |     |     |     | 15  |     |     |     |     | 5   |
| 387   | att | atc | aca | ggc | tgg | cga | ata | gga | ttt | gta | cga | gac | ata | ttg | ttt | ggc |     |
|       | Ile | Ile | Thr | Gly | Trp | Arg | Ile | Gly | Phe | Val | Arg | Asp | Ile | Leu | Phe | Gly |     |
|       |     |     | 40  |     |     |     |     | 35  |     |     |     |     | 30  |     |     |     |     |
| 435   | gga | ggt | ctg | gcc | ttt | gtt | gtt | cag | gga | att | tgc | gtt | ttt | tgc | agc | ttt |     |
|       | Gly | Gly | Leu | Ala | Phe | Val | Val | Gln | Gly | Ile | Cys | Val | Phe | Cys | Ser | Phe | 10  |
|       |     |     |     | 55  |     |     |     |     | 50  |     |     |     |     | 45  |     |     |     |
| 483   | ggg | ttt | gta | ttt | aga | gga | ttt | gaa | atg | ctg | tgg | ttt | gct | aat | ttt | ata |     |
|       | Gly | Phe | Val | Phe | Arg | Gly | Phe | Glu | Met | Leu | Trp | Phe | Ala | Asn | Phe | Ile |     |
|       |     |     |     |     | 70  |     |     |     |     | 65  |     |     |     |     | 60  |     |     |
|       |     |     |     |     |     |     |     |     |     |     |     |     |     | ggc |     |     | 15  |
|       | Ser | Val | Ala | Tyr | Thr | Asn | Gln | Ala | Val | Ala |     | Ser | Glu | Gly | Gly |     |     |
|       | 90  |     |     |     |     | 85  |     |     |     |     | 80  |     |     |     |     | 75  |     |
|       |     |     |     |     |     |     |     |     |     |     |     |     |     | aaa |     |     |     |
|       | Ser | Leu | Gln | Leu | Gly | Phe | Val | Leu | Asn | Leu | Glu |     | Gly | Lys | Phe | Trp | 0.0 |
|       |     | 105 |     |     |     |     | 100 |     |     |     |     | 95  |     |     |     |     | 20  |
|       | ctg |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|       | Leu | Trp | _   | Met | Leu | Asn | Met |     | Val | Thr | Ser | Gly |     | Arg | Ala | Met |     |
|       |     |     | 120 |     |     |     |     | 115 |     |     |     |     | 110 |     |     |     |     |
|       | ctc |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     | 25  |
|       | Leu | Thr | Thr | HlS | GLV | Ala | Ser | GLV | ьеп | ьeu | мта | GIU | тте | пAg | ser | Tyr | ر ب |

|    |     |     | 125 |     |     |     |     | 130 |     |     |     |     | 135 |     |     |     |      |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|    | ggg | atc | aca | ctt | atg | att | ggg | ggt | ata | acg | tgt | att | ctt | tca | cta | atc | 723  |
|    | Gly | Ile | Thr | Leu | Met | Ile | Gly | Gly | Ile | Thr | Суѕ | Ile | Leu | Ser | Leu | Ile |      |
|    |     | 140 |     |     |     |     | 145 |     |     |     |     | 150 |     |     |     |     |      |
| 5  | tgt | gcc | ttg | gct | ctt | gcc | tac | ttg | gat | cag | aga | gca | gag | aga | atc | ctt | 771  |
|    | Cys | Ala | Leu | Ala | Leu | Ala | Tyr | Leu | Asp | Gln | Arg | Ala | Glu | Arg | Ile | Leu |      |
|    | 155 |     |     |     |     | 160 |     |     |     |     | 165 |     |     |     |     | 170 |      |
|    | cat | aaa | gaa | caa | gga | aaa | aca | ggt | gaa | gtt | att | aaa | tta | act | gat | gta | 819  |
|    | His | Lys | Glu | Gln | Gly | Lys | Thr | Gly | Glu | Val | Ile | Lys | Leu | Thr | Asp | Val |      |
| LO |     |     |     |     | 175 |     |     |     |     | 180 |     |     |     |     | 185 |     |      |
|    | aag | gac | ttc | tcc | tta | ccc | ctg | tgg | ctt | ata | ttt | atc | atc | tgt | gtc | tgc | 867  |
|    | Lys | Asp | Phe | Ser | Leu | Pro | Leu | Trp | Leu | Ile | Phe | Ile | Ile | Cys | Val | Cys |      |
|    |     |     |     | 190 |     |     |     |     | 195 |     |     |     |     | 200 |     | •   |      |
|    | tat | tat | gtt | gct | gtg | ttc | cct | ttt | att | gga | ctt | ggg | aaa | gtt | ttc | ttt | 915  |
| 15 | Tyr | Tyr | Val | Ala | Val | Phe | Pro | Phe | Ile | Gly | Leu | Gly | Lys | Val | Phe | Phe |      |
|    |     |     | 205 |     |     |     |     | 210 |     |     |     |     | 215 |     |     |     |      |
|    | aca | gag | aaa | ttt | gga | ttt | tct | tcc | cag | gca | gca | agt | gca | att | aac | agt | 963  |
|    | Thr | Glu | Lys | Phe | Gly | Phe | Ser | Ser | Gln | Ala | Ala | Ser | Ala | Ile | Asn | Ser |      |
|    |     | 220 |     |     |     |     | 225 |     |     |     |     | 230 |     |     |     |     |      |
| 20 | gtt | gta | tat | gtc | ata | tca | gct | ccc | atg | tcc | ccg | gtg | ttt | ggg | ctc | ctg | 1011 |
|    | Val | Val | Tyr | Val | Ile | Ser | Ala | Pro | Met | Ser | Pro | Val | Phe | Gly | Leu | Leu |      |
|    | 235 |     |     |     |     | 240 |     |     |     |     | 245 |     |     |     |     | 250 |      |
|    | gtg | gat | aaa | aca | ggg | aag | aac | atc | atc | tgg | gtt | ctt | tgc | gca | gta | gca | 1059 |
|    | Val | Asp | Lys | Thr | Gly | Lys | Asn | Ile | Ile | Trp | Val | Leu | Суѕ | Ala | Val | Ala |      |
| 25 |     |     |     |     | 255 |     |     |     |     | 260 |     |     |     |     | 265 |     |      |

|    | gcc | act  | ctt | gtg  | tcc  | cac  | atg  | atg  | ctg  | gcc  | ttt  | acg | atg  | tgg | aac  | cct    | 1107 |
|----|-----|------|-----|------|------|------|------|------|------|------|------|-----|------|-----|------|--------|------|
|    | Ala | Thr  | Leu | Val  | Ser  | His  | Met  | Met  | Leu  | Ala  | Phe  | Thr | Met  | Trp | Asn  | Pro    |      |
|    |     |      |     | 270  |      |      |      |      | 275  |      |      |     |      | 280 |      |        |      |
|    | tgg | att  | gct | atg  | tgt  | ctt  | ctg  | gga  | ctc  | tcc  | tac  | tca | ttg  | ctt | gcc  | tgt    | 1155 |
| 5  | Trp | Ile  | Ala | Met  | Cys  | Leu  | Leu  | Gly  | Leu  | Ser  | Tyr  | Ser | Leu  | Leu | Ala  | Cys    |      |
|    |     |      | 285 |      |      |      |      | 290  |      |      |      |     | 295  |     |      |        |      |
|    | gca | ttg  | tgg | cca  | atg  | gtg  | gca  | ttt  | gta  | gtt  | cct  | gaa | cat  | cag | ctg  | gga    | 1203 |
|    | Ala | Leu  | Trp | Pro  | Met  | Val  | Ala  | Phe  | Val  | Val  | Pro  | Glu | His  | Gln | Leu  | Gly    |      |
|    |     | 300  |     |      |      |      | 305  |      |      |      |      | 310 |      |     |      |        |      |
| 10 | act | gca  | tat | ggc  | ttc  | atg  | cag  | tcc  | att  | cag  | aat  | ctt | ggg  | ttg | gcc  | atc    | 1251 |
|    | Thr | Ala  | Tyr | Gly  | Phe  | Met  | Gln  | Ser  | Ile  | Gln  | Asn  | Leu | Gly  | Leu | Ala  | Ile    |      |
|    | 315 |      |     |      |      | 320  |      |      |      |      | 325  |     |      |     |      | 330    |      |
|    | att | tcc  | atc | att  | gct  | ggt  | atg  | ata  | ctg  | gat  | tct  | cgg | ggg  | tat | ttg  | ttt    | 1299 |
|    | Ile | Ser  | Ile | Ile  | Ala  | Gly  | Met  | Ile  | Leu  | Asp  | Ser  | Arg | Gly  | Tyr | Leu  | Phe    |      |
| 15 |     |      |     |      | 335  |      |      |      |      | 340  |      |     |      |     | 345  |        |      |
|    | ttg | gaa  | gtg | ttc  | ttc  | att  | gcc  | tgt  | gtt  | tct  | ttg  | tca | ctt  | tta | tct  | gtg    | 1347 |
|    | Leu | Glu  | Val | Phe  | Phe  | Ile  | Ala  | Cys  | Val  | Ser  | Leu  | Ser | Leu  | Leu | Ser  | Val    |      |
|    |     |      |     | 350  |      |      |      |      | 355  |      |      |     |      | 360 |      |        |      |
|    | gtc | tta  | ctc | tat  | ttg  | gtg  | aat  | cgt  | gcc  | cag  | ggt  | ggg | aac  | cta | aat  | tat    | 1395 |
| 20 | Val | Leu  | Leu | Tyr  | Leu  | Val  | Asn  | Arg  | Ala  | Gln  | Gly  | Gly | Asn  | Leu | Asn  | Tyr    |      |
|    |     |      | 365 |      |      |      |      | 370  |      |      |      |     | 375  |     |      |        |      |
|    | tct | gca  | aga | caa  | agg  | gaa  | gaa  | ata  | aaa  | ttt  | tcc  | cat | act  | gaa | tga  |        | 1440 |
|    | Ser | Ala  | Arg | Gln  | Arg  | Glu  | Glu  | Ile  | ГÀг  | Phe  | Ser  | His | Thr  | Glu | l    |        |      |
|    |     | 380  |     |      |      |      | 385  |      |      |      |      | 390 |      |     |      |        |      |
| 25 | gaa | gtta | aaa | tgaa | tgtg | tc a | tgag | aatg | g gc | ttaa | caca | tcg | ttgg | ttt | gaaa | acttcc | 1500 |

atttttaaaa atttagagtt tagtcattag aaaaaataat ggactggaaa gttatattta 1560 tatccaaata tacctatttc aaagtgtatt tgtgaggcct gttttagcct gtgtcttttg 1620 tattgtgtgt tgctaaagaa ttctactttt agtaggctaa tcaacaatga aagggttaga 1680 aaattgctgt ggaacatcca ggtgaacttc aggaaagaca gtgaaaaatg gaaaacgttg 1740 gagettetgt tgagataate tteattaggt atatatetta gggatacage etttetta 1800 tettatagea ggaaaaaaaa aettttgagg gaaatagaag ggetgegtta cacaaaataa 1860 acaatggcat tgtcataggc cttcctttta ctagtagggc ataatgctag ggaatatgtg 1920 aagatgtttt tatgaagtct ctttctgatc acgaacaata gcttgcgctc tactctgtag 1980 ttatgtggat tgccgagcaa tgaccctttt caatttctta tttctgtgtt actgaggacc 2040 10 ctaatcactt agggatgtaa ttttatagta taaactttct gtacagtttt tcttatagtc 2100 taataagtaa aaagtgtcct tcaaattatg ataattgcct atgtacatgg ataaattaaa 2160 acactgcaca cgg 2173

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20 <221> CDS

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|    |     |     |     |     |     |      |     |     | 1   | Ĺ   |     |     | ;   | 5   |     |     |     |
|----|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | ctg | ccc | ctt | ttc | ttc | ttc  | tgc | tgg | gag | gtt | ggg | gtc | tct | ggg | agc | tct | 102 |
|    | Leu | Pro | Leu | Phe | Phe | Phe  | Cys | Trp | Glu | Val | Gly | Val | Ser | Gly | Ser | Ser |     |
|    |     | 10  |     |     |     |      | 15  |     |     |     |     | 20  |     |     |     |     |     |
| 5  | gca | ggc | ccc | agc | acc | cgc  | aga | gca | gac | act | gcg | atg | aca | acg | gac | gac | 150 |
|    | Ala | Gly | Pro | Ser | Thr | Arg  | Arg | Ala | Asp | Thr | Ala | Met | Thr | Thr | Asp | Asp |     |
|    | 25  |     |     |     |     | 30   |     |     |     |     | 35  |     |     |     |     | 40  |     |
|    | aca | gaa | gtg | ccc | gct | atg  | act | cta | gca | ccg | ggc | cac | gcc | gct | ctg | gaa | 198 |
|    | Thr | Glu | Val | Pro | Ala | Met  | Thr | Leu | Ala | Pro | Gly | His | Ala | Ala | Leu | Glu |     |
| 10 |     |     |     |     | 45  |      |     |     |     | 50  |     |     |     |     | 55  |     |     |
|    | act | caa | acg | ctg | agc | gct  | gag | acc | tct | tct | agg | gcc | tca | acc | cca | gcc | 246 |
|    | Thr | Gln | Thr | Leu | Ser | Ala  | Glu | Thr | Ser | Ser | Arg | Ala | Ser | Thr | Pro | Ala |     |
| •  |     |     |     | 60  |     |      |     |     | 65  |     |     |     |     | 70  |     |     |     |
|    | ggc | ccc | att | cca | gaa | gca  | gag | acc | agg | gga | gcc | aag | aga | att | tcc | cct | 294 |
| 15 | Gly | Pro | Ile | Pro | Glu | Ala  | Glu | Thr | Arg | Gly | Ala | Lys | Arg | Ile | Ser | Pro |     |
|    |     |     | 75  |     |     |      |     | 80  |     |     |     |     | 85  |     |     |     |     |
|    | gca | aga | gag | acc | agg | agt  | ttc | aca | aaa | aca | tct | ccc | aac | ttc | atg | gtg | 342 |
|    | Ala | Arg | Glu | Thr | Arg | Ser  | Phe | Thr | Lys | Thr | Ser | Pro | Asn | Phe | Met | Val |     |
|    |     | 90  |     |     |     |      | 95  |     |     |     |     | 100 |     |     |     |     |     |
| 20 | ctg | atc | gcc | acc | tcc | gtg  | gag | aca | tca | gcc | gcc | agt | ggc | agc | ccc | gag | 390 |
|    | Leu | Ile | Ala | Thr | Ser | Val  | Glu | Thr | Ser | Ala | Ala | Ser | Gly | Ser | Pro | Glu |     |
|    | 105 |     |     |     |     | 110  |     |     |     |     | 115 |     |     |     |     | 120 |     |
|    | gga | gct | gga | atg | acc | a.ca | gtt | cag | acc | atc | aca | ggc | agt | gat | ccc | gag | 438 |
|    | Gly | Ala | Gly | Met | Thr | Thr  | Val | Gln | Thr | Ile | Thr | Gly | Ser | Asp | Pro | Glu |     |
| 25 |     |     |     |     | 125 |      |     |     |     | 130 |     |     |     |     | 135 |     |     |

|    | gaa | gcc | atc | ttt | gac | acc | ctt | tgc | acc | gat | gac | agc | tct | gaa | gag | gca | 486 |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Glu | Ala | Ile | Phe | Asp | Thr | Leu | Cys | Thr | Asp | Asp | Ser | Ser | Glu | Glu | Ala |     |
|    |     |     |     | 140 |     |     |     |     | 145 |     |     |     |     | 150 |     |     |     |
|    | aag | aca | ctc | aca | atg | gac | ata | ttg | aca | ttg | gct | cac | acc | tcc | aca | gaa | 534 |
| 5  | Lys | Thr | Leu | Thr | Met | Asp | Ile | Leu | Thr | Leu | Ala | His | Thr | Ser | Thr | Glu |     |
|    |     |     | 155 |     |     |     |     | 160 |     |     |     |     | 165 |     |     |     |     |
|    | gct | aag | ggc | ctg | tcc | tca | gag | agc | agt | gcc | tct | tcc | gac | ggc | ccc | cat | 582 |
|    | Ala | Lys | Gly | Leu | Ser | Ser | Glu | Ser | Ser | Ala | Ser | Ser | Asp | Gly | Pro | His |     |
|    |     | 170 |     |     |     |     | 175 |     |     |     |     | 180 |     |     |     |     |     |
| 10 | cca | gtc | atc | acc | ccg | tca | cgg | gcc | tca | gag | agc | agc | gcc | tct | tcc | gac | 630 |
|    | Pro | Val | Ile | Thr | Pro | Ser | Arg | Ala | Ser | Glu | Ser | Ser | Ala | Ser | Ser | Asp |     |
|    | 185 |     |     |     |     | 190 |     |     |     |     | 195 |     |     |     |     | 200 |     |
|    | ggc | ccc | cat | сса | gtc | atc | acc | ccg | tca | cgg | gcc | tca | gag | agc | agc | gcc | 678 |
|    | Gly | Pro | His | Pro | Val | Ile | Thr | Pro | Ser | Arg | Ala | Ser | Glu | Ser | Ser | Ala |     |
| 15 |     | •   |     |     | 205 |     |     |     |     | 210 |     |     |     |     | 215 |     |     |
|    | tct | tcc | gac | ggc | ccc | cat | cca | gtc | atc | acc | ccc | tca | tgg | tcc | ccg | gga | 726 |
|    | Ser | Ser | Asp | Gly | Pro | His | Pro | Val | Ile | Thr | Pro | Ser | Trp | Ser | Pro | Gly |     |
|    |     |     |     | 220 |     |     |     |     | 225 |     |     |     |     | 230 |     | •   |     |
|    | tct | gat | gtc | act | ctc | ctc | gct | gaa | gcc | ctg | gtg | act | gtc | aca | aac | atc | 774 |
| 20 | Ser | Asp | Val | Thr | Leu | Leu | Ala | Glu | Ala | Leu | Val | Thr | Val | Thr | Asn | Ile |     |
|    |     |     | 235 |     |     |     |     | 240 |     |     |     |     | 245 |     |     |     |     |
|    | gag | gtt | att | aat | tgc | agc | atc | aca | gaa | ata | gaa | aca | aca | act | tcc | agc | 822 |
|    | Glu | Val | Ile | Asn | Cys | Ser | Ile | Thr | Glu | Ile | Glu | Thr | Thr | Thr | Ser | Ser |     |
|    |     | 250 |     |     |     |     | 255 |     |     |     |     | 260 |     |     |     |     |     |
| 25 | atc | cct | ggg | gcc | tca | gac | ata | gat | ctc | atc | ccc | acg | gaa | ggg | gtg | aag | 870 |

|    | Ile | Pro | Gly | Ala | Ser | Asp | Ile | Asp | Leu | Ile | Pro | Thr | Glu | Gly | Val | Lys   |      |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------|------|
|    | 265 |     |     |     |     | 270 |     |     |     |     | 275 |     |     |     |     | 280   |      |
|    | gcc | tcg | tcc | acc | tcc | gat | cca | cca | gct | ctg | cct | gac | tcc | act | gaa | gca   | 918  |
|    | Ala | Ser | Ser | Thr | Ser | Asp | Pro | Pro | Ala | Leu | Pro | Asp | Ser | Thr | Glu | Ala   |      |
| 5  |     |     |     |     | 285 |     |     |     |     | 290 |     |     |     |     | 295 |       |      |
|    | aaa | cca | cac | atc | act | gag | gtc | aca | gcc | tct | gcc | gag | acc | ctg | tcc | aca   | 966  |
|    | Lys | Pro | His | Ile | Thr | Glu | Val | Thr | Ala | Ser | Ala | Glu | Thr | Leu | Ser | Thr   |      |
|    |     |     |     | 300 |     |     |     |     | 305 |     |     |     |     | 310 |     |       |      |
|    | gcc | ggc | acc | aca | gag | tca | gct | gca | cct | cat | gcc | acg | gtt | ggg | acc | cca   | 1014 |
| 10 | Ala | Gly | Thr | Thr | Glu | Ser | Ala | Ala | Pro | His | Ala | Thr | Val | Gly | Thr | Pro   |      |
|    |     |     | 315 |     |     |     |     | 320 |     | ٥   |     |     | 325 |     |     |       |      |
|    | ctc | ccc | act | aac | agc | gcc | aca | gaa | aga | gaa | gtg | aca | gca | ccc | ggg | gcc   | 1062 |
|    | Leu | Pro | Thr | Asn | Ser | Ala | Thr | Glu | Arg | Glu | Val | Thr | Ala | Pro | Gly | Ala   |      |
|    |     | 330 |     |     |     |     | 335 |     |     |     |     | 340 |     |     |     |       |      |
| 15 | acg | acc | ctc | agt | gga | gct | ctg | gtc | aca | gtt | agc | agg | aat | ccc | ctg | gaa   | 1110 |
|    | Thr | Thr | Leu | Ser | Gly | Ala | Leu | Val | Thr | Val | Ser | Arg | Asn | Pro | Leu | Glu   |      |
|    | 345 |     |     |     |     | 350 |     |     |     |     | 355 |     |     |     |     | 360   |      |
|    | gaa | acc | tca | gcc | ctc | tct | gtt | gag | aca | cca | agt | tac | gtc | aaa | gtc | tca   | 1158 |
|    | Glu | Thr | Ser | Ala | Leu | Ser | Val | Glu | Thr | Pro | Ser | Tyr | Val | Lys | Val | Ser   |      |
| 20 |     |     |     |     | 365 |     |     |     |     | 370 |     |     |     |     | 375 |       |      |
|    | gga | gca | gct | ccg | gtc | tcc | ata | gag | gct | ggg | tca | gca | gtg | ggc | aaa | aca   | 1206 |
|    | Gly | Ala | Ala | Pro | Val | Ser | Ile | Glu | Ala | Gly | Ser | Ala | Val | Gly | Lys | Thr . |      |
|    |     |     |     | 380 |     |     |     |     | 385 |     |     |     |     | 390 |     |       |      |
|    | act | tcc | ttt | gct | ggg | agc | tct | gct | tcc | tcc | tac | agc | ccc | tcg | gaa | gcc   | 1254 |
| 25 | Thr | Ser | Phe | Ala | Gly | Ser | Ser | Ala | Ser | Ser | Tyr | Ser | Pro | Ser | Glu | Ala   |      |

|    |     |     | 395 |     |     |     |     | 400 |     |     |     |     | 405 |     |     |     |      |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|    | gcc | ctc | aag | aac | ttc | acc | cct | tca | gag | aca | ccg | acc | atg | gac | atc | gca | 1302 |
|    | Ala | Leu | Lys | Asn | Phe | Thr | Pro | Ser | Glu | Thr | Pro | Thr | Met | Asp | Ile | Ala |      |
|    |     | 410 |     |     |     |     | 415 |     |     |     |     | 420 |     |     |     |     |      |
| 5  | acc | aag | ggg | ccc | ttc | ccc | acc | agc | agg | gac | cct | ctt | cct | tct | gtc | cct | 1350 |
|    | Thr | Lys | Gly | Pro | Phe | Pro | Thr | Ser | Arg | Asp | Pro | Leu | Pro | Ser | Val | Pro |      |
|    | 425 |     |     |     |     | 430 |     |     |     |     | 435 |     |     |     |     | 440 |      |
|    | ccg | act | aca | acc | aac | agc | agc | cga | ggg | acg | aac | agc | acc | tta | gcc | aag | 1398 |
|    | Pro | Thr | Thr | Thr | Asn | Ser | Ser | Arg | Gly | Thr | Asn | Ser | Thr | Leu | Ala | Lys |      |
| 10 |     |     |     |     | 445 |     |     |     |     | 450 |     |     |     |     | 455 |     |      |
|    | atc | aca | acc | tca | gcg | aag | acc | acg | atg | aag | ccc | cca | aca | gcc | acg | ccc | 1446 |
|    | Ile | Thr | Thr | Ser | Ala | Lys | Thr | Thr | Met | Lys | Pro | Pro | Thr | Ala | Thr | Pro |      |
|    |     |     |     | 460 |     |     |     |     | 465 |     |     |     |     | 470 |     |     |      |
|    | acg | act | gcc | cgg | acg | agg | ccg | acc | aca | gac | gtg | agt | gca | ggt | gaa | aat | 1494 |
| 15 | Thr | Thr | Ala | Arg | Thr | Arg | Pro | Thr | Thr | Asp | Val | Ser | Ala | Gly | Glu | Asn |      |
|    |     |     | 475 |     |     |     |     | 480 |     |     |     |     | 485 |     |     |     |      |
|    | gga | ggt | ttc | ctc | ctc | ctg | cgg | ctg | agt | gtg | gct | tcc | ccg | gaa | gac | ctc | 1542 |
|    | Gly | Gly | Phe | Leu | Leu | Leu | Arg | Leu | Ser | Val | Ala | Ser | Pro | Glu | Asp | Leu |      |
|    |     | 490 |     |     |     |     | 495 |     |     |     |     | 500 |     |     |     |     |      |
| 20 | act | gac | ccc | aga | gtg | gca | gaa | agg | ctg | atg | cag | cag | ctc | cac | cgg | gaa | 1590 |
|    | Thr | Asp | Pro | Arg | Val | Ala | Glu | Arg | Leu | Met | Gln | Gln | Leu | His | Arg | Glu |      |
|    | 505 |     |     |     |     | 510 |     |     |     |     | 515 |     |     |     |     | 520 |      |
|    | ctc | cac | gcc | cac | gcg | cct | cac | ttc | cag | gtc | tcc | tta | ctg | cgt | gtc | agg | 1638 |
|    | Leu | His | Ala | His | Ala | Pro | His | Phe | Gln | Val | Ser | Leu | L u | Arg | Val | Arg |      |
| 25 |     |     |     |     | 525 |     |     |     |     | 530 |     |     |     |     | 535 |     |      |

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aga ggc taa cggacatcag ctgcagccag gcatgtcccg tatgccaaaa 1687
Arg Gly
gagggtgctg cccctagcct gggcccccac cgacagactg cagctgcgtt actgtgctga 1747
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caacaggacc ctcgctcaca tccaccggag tgtatgtatg gggaggggct tcacctgttc 1867
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Met Glu Ala Ala Leu Leu Gly Leu Cys Asn Trp Ser Thr

1 5 10

ctg ggc gtg tgc gcc gcg ctg aag ctg ccg cag atc tcc gct gtg cta 157 Leu Gly Val Cys Ala Ala Leu Lys Leu Pro Gln Ile Ser Ala Val Leu

25 15 20 25

|    | gcg  | gcg   | cgc   | agc   | gcg   | cgg   | ggc   | ctc   | agc   | ctt   | ccg  | agt  | tta   | ctt   | ctg   | gag    | 205 |
|----|------|-------|-------|-------|-------|-------|-------|-------|-------|-------|------|------|-------|-------|-------|--------|-----|
|    | Ala  | Ala   | Arg   | Ser   | Ala   | Arg   | Gly   | Leu   | Ser   | Leu   | Pro  | Ser  | Leu   | Leu   | Leu   | Glu    |     |
|    | 30   |       |       |       |       | 35    |       |       |       |       | 40   |      |       |       |       | 45     |     |
|    | ctg  | gca   | gga   | ttc   | ctg   | gtg   | ttt   | ctg   | cgg   | tac   | cag  | tgt  | tac   | tat   | ggg   | tat    | 253 |
| 5  | Leu  | Ala   | Gly   | Phe   | Leu   | Val   | Phe   | Leu   | Arg   | Tyr   | Gln  | Cys  | Tyr   | Tyr   | Gly   | Tyr    |     |
|    |      |       |       |       | 50    |       |       |       |       | 55    |      |      |       |       | 60    |        |     |
|    | ccg  | ccg   | ctg   | acc   | tac   | ctg   | gag   | tac   | ccc   | atc   | ctc  | atc  | gcg   | caa   | gat   | gtc    | 301 |
|    | Pro  | Pro   | Leu   | Thr   | Tyr   | Leu   | Glu   | Tyr   | Pro   | Ile   | Leu  | Ile  | Ala   | Gln   | Asp   | Val    |     |
|    |      |       |       | 65    |       |       |       |       | 70    |       |      |      |       | 75    |       |        |     |
| 10 | atc  | ctc   | ctg   | ctc   | tgt   | atc   | ttt   | cat   | ttt   | aac   | ggg  | aac  | gtg   | aag   | cag   | gcc    | 349 |
|    | Ile  | Leu   | Leu   | Leu   | Cys   | Ile   | Phe   | His   | Phe   | Asn   | Gly  | Asn  | Val   | Lys   | Gln   | Ala    |     |
|    |      |       | 80    |       |       |       |       | 85    |       |       |      |      | 90    |       |       |        |     |
|    | act  | cct   | tac   | atc   | gct   | gtg   | tat   | cct   | ttc   | tga   | atct | gago | cca q | gaag  | tggga | aa     | 399 |
|    | Thr  | Pro   | Tyr   | Ile   | Ala   | Val   | Tyr   | Pro   | Phe   |       |      |      |       |       |       |        |     |
| 15 |      | 95    |       |       |       |       | 100   |       |       |       |      |      |       |       |       |        |     |
|    | cggg | ggato | gtt a | attt  | gcgaa | at gt | agag  | gacgo | g tgt | ttc   | geeg | tgci | tggc  | cag ( | gatgo | gtctcg | 459 |
|    | atct | tect  | gac d | ctcat | gato  | ct go | cctgo | ctc   | g gcd | ctcc  | cagg | gtg  | ctgga | aat 1 | tacag | ggtgtg | 519 |
|    | agco | cacc  | gca ( | cctg  | geete | ct tt | tgct  | tttt  | taa   | acaa  | atcg | acto | cgtga | act ' | ttcto | cacatt | 579 |
|    | ttat | tctg  | caa a | acaga | atct  | a to  | gtact | ttca  | a tca | agcgo | cggc | cagi | taagt | tt    | gcaca | agctcc | 639 |
| 20 | agto | gtct  | gtg ( | gaaga | acgag | ga ga | actca | aggaa | a cto | gtgag | gtgc | gct  | gacti | tgg a | agcct | tctctt | 699 |
|    | ccta | atac  | ctg 1 | tgcaa | acaaç | ga at | caato | cacaa | a cct | taat  | tgac | cac  | caat  | gat ' | tttad | caattc | 759 |
|    | ttc  | tacgi | ttt 1 | tgtga | atcat | g ct  | cggct | ttaa  | a ata | atato | gggt | aaca | agtga | aca ( | gtact | ttcgct | 819 |
|    | acc  | ggaa  | gac ( | cgcta | ataaa | ag go | ctgaa | atgat | gga   | ataca | atta | ttc  | cttca | aca   | cagt  | ggattt | 879 |
|    | tga  | gtaad | ctg a | aacca | aaago | ga aa | aaaga | agct  | ctt   | tgcl  | taaa | ttaa | aggto | ctt   | ttata | aaattt | 939 |
| 25 | agta | aaato | cag 1 | tttai | taato | t tt  | taaaq | gccaa | a ago | tttt  | tttt | agad | cttga | aaa ( | gaaaq | gagcca | 999 |

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|----|-----|------|-----|------|------|-------|------|------|------|------|------|-----|------|-----|------|-------|-----|
|    | aga | gcag | gcc | tggt | ggtg | ag ca | aggg | acgg | t gc | accg | gacg | gcg | ggat | cga | gcaa | atg   | 57  |
|    |     |      |     |      |      |       |      |      |      |      |      |     |      |     |      | Met   |     |
|    |     |      |     |      |      |       |      |      |      |      |      |     |      |     |      | 1     |     |
| 5  | ggt | ctg  | gcc | atg  | gag  | cac   | gga  | ggg  | tcc  | tac  | gct  | cgg | gcg  | ggg | ggc  | agc   | 105 |
|    | Gly | Leu  | Ala | Met  | Glu  | His   | Gly  | Gly  | Ser  | Tyr  | Ala  | Arg | Ala  | Gly | Gly  | Ser   |     |
|    |     |      |     | 5    |      |       |      |      | 10   |      |      |     |      | 15  |      |       |     |
|    | tct | cgg  | ggc | tgc  | tgg  | tat   | tac  | ctg  | cgc  | tac  | ttc  | ttc | ctc  | ttc | gtc  | tcc   | 153 |
|    | Ser | Arg  | Gly | Cys  | Trp  | Tyr   | Tyr  | Leu  | Arg  | Tyr  | Phe  | Phe | Leu  | Phe | Val  | Ser   |     |
| 10 |     |      | 20  |      |      |       |      | 25   |      |      |      |     | 30   |     |      |       |     |
|    | ctc | atc  | caa | ttc  | ctc  | atc   | atc  | ctg  | ggg  | ctc  | gtg  | ctc | ttc  | atg | gtc  | tat   | 201 |
|    | Leu | Ile  | Gln | Phe  | Leu  | Ile   | Ile  | Leu  | Gly  | Leu  | Val  | Leu | Phe  | Met | Val  | Tyr   |     |
|    |     | 35   |     |      |      |       | 40   |      |      |      |      | 45  |      |     |      |       |     |
|    | ggc | aac  | gtg | cac  | gtg  | agc   | aca  | gag  | tcc  | aac  | ctg  | cag | gcc  | acc | gag  | cgc . | 249 |
| 15 | Gly | Asn  | Val | His  | Val  | Ser   | Thr  | Glu  | Ser  | Asn  | Leu  | Gln | Ala  | Thr | Glu  | Arg   |     |
|    | 50  |      |     |      |      | 55    |      |      |      |      | 60   |     |      |     |      | 65    |     |
|    | cga | gcc  | gag | ggc  | cta  | tac   | agt  | cag  | ctc  | cta  | ggg  | ctc | acg  | gcc | tcc  | cag   | 297 |
|    | Arg | Ala  | Glu | Gly  | Leu  | Tyr   | Ser  | Gln  | Leu  | Leu  | Gly  | Leu | Thr  | Ala | Ser  | Gln   |     |
|    |     |      |     |      | 70   |       |      |      |      | 75   |      |     |      |     | 80   |       |     |
| 20 | tcc | aac  | ttg | acc  | aag  | gag   | ctc  | aac  | ttc  | acc  | acc  | cgc | gcc  | aag | gat  | gcc   | 345 |
|    | Seŗ | Asn  | Leu | Thr  | Lys  | Glu   | Leu  | Asn  | Phe  | Thr  | Thr  | Arg | Ala  | Lys | Asp  | Ala   |     |
|    |     |      |     | 85   |      |       |      |      | 90   | •    |      |     |      | 95  |      |       |     |
|    | atc | atg  | cag | atg  | tgg  | ctg   | aat  | gct  | cgc  | cgc  | gac  | ctg | gac  | cgc | atc  | aat   | 393 |
|    | Ile | Met  | Gln | Met  | Trp  | Leu   | Asn  | Ala  | Arg  | Arg  | Asp  | Leu | Asp  | Arg | Ile  | Asn   |     |
| 25 |     |      | 100 |      |      |       |      | 105  |      |      |      |     | 110  |     |      |       |     |

|    | gcc | agc | ttc | cgc | cag | tgc | cag | ggt | gac | cgg | gtc | atc | tac | acg | aac | aat | 441 |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Ala | Ser | Phe | Arg | Gln | Cys | Gln | Gly | Asp | Arg | Val | Ile | Tyr | Thr | Asn | Asn |     |
|    |     | 115 |     |     |     | •   | 120 |     |     |     |     | 125 |     |     |     |     |     |
|    | cag | agg | tac | atg | gct | gcc | atc | atc | ttg | agt | gag | aag | caa | tgc | aga | gat | 489 |
| 5  | Gln | Arg | Tyr | Met | Ala | Ala | Ile | Ile | Leu | Ser | Glu | Lys | Gln | Cys | Arg | Asp |     |
|    | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     | 145 |     |
|    | caa | ttc | aag | gac | atg | aac | aag | agc | tgc | gat | gcc | ttg | ctc | ttc | atg | ctg | 537 |
|    | Gln | Phe | Lys | Asp | Met | Asn | Lys | Ser | Cys | Asp | Ala | Leu | Leu | Phe | Met | Leu |     |
|    |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |     |     |
| 10 | aat | cag | aag | gtg | aag | acg | ctg | gag | gtg | gag | ata | gcc | aag | gag | aag | acc | 585 |
|    | Asn | Gln | Lys | Val | Lys | Thr | Leu | Glu | Val | Glu | Ile | Ala | Lys | Glu | Lys | Thr |     |
|    |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |     |     |
|    | att | tgc | act | aag | gat | aag | gaa | agc | gtg | ctg | ctg | aac | aaa | cgc | gtg | gcg | 633 |
|    | Ile | Cys | Thr | Lys | Asp | Lys | Glu | Ser | Val | Leu | Leu | Asn | Lys | Arg | Val | Ala |     |
| 15 |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |     |     |
|    | gag | gaa | cag | ctg | gtt | gaa | tgc | gtg | aaa | acc | cgg | gag | ctg | cag | cac | caa | 681 |
|    | Glu | Glu | Gln | Leu | Val | Glu | Cys | Val | Lys | Thr | Arg | Glu | Leu | Gln | His | Gln | •   |
|    |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |     |     |
|    | gag | cgc | cag | ctg | gcc | aag | gag | caa | ctg | caa | aag | gtg | caa | gcc | ctc | tgc | 729 |
| 20 | Glu | Arg | Gln | Leu | Ala | Lys | Glu | Gln | Leu | Gln | Lys | Val | Gln | Ala | Leu | Cys |     |
|    | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     | 225 |     |
|    | ctg | ccc | ctg | gac | aag | gac | aag | ttt | gag | atg | gac | ctt | cgt | aac | ctg | tgg | 777 |
|    | Leu | Pro | Leu | Asp | Lys | Asp | Lys | Phe | Glu | Met | Asp | Leu | Arg | Asn | Leu | Trp |     |
|    |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |     |     |
| 25 | agg | gac | tcc | att | atc | cca | cgc | agc | ctg | gac | aac | ctg | ggt | tac | aac | ctc | 825 |
|    |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |

|    | Arg | Asp | Ser | Ile | Ile | Pro | Arg | Ser | Leu | Asp | Asn | Leu | Gly | Tyr | Asn | Leu |      |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|    |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |     |      |
|    | tac | cat | ccc | ctg | ggc | tcg | gaa | ttg | gcc | tcc | atc | cgc | aga | gcc | tgc | gac | 873  |
|    | Tyr | His | Pro | Leu | Gly | Ser | Glu | Leu | Ala | Ser | Ile | Arg | Arg | Ala | Cys | Asp |      |
| 5  |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |     |      |
|    | cac | atg | ccc | agc | ctc | atg | agc | tcc | aag | gtg | gag | gag | ctg | gcc | cgg | agc | 921  |
|    | His | Met | Pro | Ser | Leu | Met | Ser | Ser | Lys | Val | Glu | Glu | Leu | Ala | Arg | Ser |      |
|    |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |     |      |
|    | ctc | cgg | gcg | gat | atc | gaa | cgc | gtg | gcc | cgc | gag | aac | tca | gac | ctc | caa | 969  |
| 10 | Leu | Arg | Ala | Asp | Ile | Glu | Arg | Val | Ala | Arg | Glu | Asn | Ser | Asp | Leu | Gln |      |
|    | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     | 305 |      |
|    | cgc | cag | aag | ctg | gaa | gcc | cag | cag | ggc | ctg | cgg | gcc | agt | cag | gag | gcg | 1017 |
|    | Arg | Gln | Lys | Leu | Glu | Ala | Gln | Gln | Gly | Lęu | Arg | Ala | Ser | Gln | Glu | Ala |      |
|    |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |     |      |
| 15 | aaa | cag | aag | gtg | gag | aag | gag | gct | cag | gcc | cgg | gag | gcc | aag | ctc | caa | 1065 |
|    | Lys | Gln | Lys | Val | Glu | Lys | Glu | Ala | Gln | Ala | Arg | Glu | Ala | Lys | Leu | Gln |      |
|    |     |     |     | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |     |      |
|    | gct | gaa | tgc | tcc | cgg | cag | acc | cag | cta | gcg | ctg | gag | gag | aag | gcg | gtg | 1113 |
|    | Ala | Glu | Cys | Ser | Arg | Gln | Thr | Gln | Leu | Ala | Leu | Glu | Glu | Lys | Ala | Val |      |
| 20 |     |     | 340 |     |     |     |     | 345 |     |     |     | •   | 350 |     |     |     |      |
|    | ctg | cgg | aag | gaa | cga | gac | aac | ctg | gcc | aag | gag | ctg | gaa | gag | aag | aag | 1161 |
|    | Leu | Arg | Lys | Glu | Arg | Asp | Asn | Leu | Ala | Lys | Glu | Leu | Glu | Glu | Lys | Lys |      |
|    |     | 355 |     |     |     |     | 360 |     |     |     |     | 365 |     |     |     |     |      |
|    | agg | gag | gcg | gag | cag | ctc | agg | atg | gag | ctg | gcc | ato | aga | aac | tca | gcc | 1209 |
| 25 | Arg | Glu | Ala | Glu | Gln | Leu | Arg | Met | Glu | Leu | Ala | lle | Arg | Asn | Ser | Ala |      |

|    | 370       |              | 375           | 380          |                 | 385         |
|----|-----------|--------------|---------------|--------------|-----------------|-------------|
|    | ctg gac a | acc tgc atc  | aag acc aag   | tcg cag ccg  | atg atg cca gtg | tca 1257    |
|    | Leu Asp T | Thr Cys Ile  | Lys Thr Lys   | Ser Gln Pro  | Met Met Pro Val | Ser         |
|    |           | 390          |               | 395          | 400             |             |
| 5  | agg ccc a | atg ggc cct  | gtc ccc aac   | ccc cag ccc  | atc gac cca gct | agc 1305    |
|    | Arg Pro M | Met Gly Pro  | Val Pro Asn   | Pro Gln Pro  | Ile Asp Pro Ala | Ser         |
|    |           | 405          |               | 410          | 415             |             |
|    | ctg gag g | gag ttc aag  | agg aag atc   | ctg gag tcc  | cag agg ccc cct | gca 1353    |
|    | Leu Glu G | Glu Phe Lys  | Arg Lys Ile   | Leu Glu Ser  | Gln Arg Pro Pro | Ala         |
| 10 | 4         | 420          | 425           |              | 430             |             |
|    | ggc atc c | ect gta gec  | cca tcc agt   | ggc tga ggag | gctcca ggcctgag | ga 1403     |
|    | Gly Ile E | Pro Val Ala  | Pro Ser Ser   | Gly          |                 |             |
|    | 435       |              | 440           | •            |                 |             |
|    | ccaagggat | tg gcccgacto | g geggtttgeg  | gaģgatgcag   | ggatatgctc acag | cgcccg 1463 |
| 15 | acacaacco | cc ctcccgccg | c ccccaaccac  | ccagggccac   | catcagacaa ctcc | ctgcat 1523 |
|    | gcaaaccc  | ct agtacccto | t cacacccgca  | cccgcgcctc   | acgatecete acce | agagca 1583 |
|    | cacggccgc | cg gagatgacg | rt cacgcaagca | acggcgctga   | cgtcacatat cacc | gtggtg 1643 |
|    | atggcgtca | ac gtggccato | rt agacgtcacg | aagagatata   | gcgatggcgt cgtg | cagatg 1703 |
|    | cagcacgto | cg cacacagad | a tggggaactt  | ggcatgacgt   | cacaccgaga tgca | gcaacg 1763 |
| 20 | acgtcacgg | gg ccatgtcga | c gtcacacata  | ttaatgtcac   | acagacgcgg cgat | ggcatc 1823 |
|    | acacagaco | gg tgatgatgt | c acacacagad  | : acagtgacaa | cacacaccat gaca | acgaca 1883 |
|    | cctatagat | ta tggcaccaa | c atcacatgca  | cgcatgccct   | ttcacacaca cttt | ctaccc 1943 |
|    | aattctcac | cc tagtgtcad | g ttccccgad   | cctggcacac   | gggccaaggt accc | acagga 2003 |
|    | tcccatcc  | cc tcccgcaca | g ccctgggcc   | cagcacctcc   | cctcctccag cttc | ctggcc 2063 |
| 25 | tcccagcca | ac ttcctcaco | c ccagtgcctg  | gacccggagg   | tgagaacagg aagc | cattca 2123 |

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cetecgetee ttgagegtga gtgttteeag gaeeeeeteg gggeeetgag eeggggtga 2183
gggteacetg ttgtegggag gggageeact cetteteece caacteeeag eeetgeetgt 2243
ggeeegttga aatgttggtg geacttaata aatattagta aateetteaa ag 2295

5 <210> 91

<211> 227

<212> PRT

<213> Homo sapiens

10 <400> 91

Met Ala Gly Val Gly Ala Gly Pro Leu Arg Ala Met Gly Arg Gln Ala

5 10 15

Leu Leu Leu Ala Leu Cys Ala Thr Gly Ala Gln Gly Leu Tyr Phe

20 25 30

15 His Ile Gly Glu Thr Glu Lys Arg Cys Phe Ile Glu Glu Ile Pro Asp

35 40 45

Glu Thr Met Val Ile Gly Asn Tyr Arg Thr Gln Met Trp Asp Lys Gln
50 55 60

Lys Glu Val Phe Leu Pro Ser Thr Pro Gly Leu Gly Met His Val Glu

20 65 70 75 80

Val Lys Asp Pro Asp Gly Lys Val Val Leu Ser Arg Gln Tyr Gly Ser

85 90 95

Glu Gly Arg Phe Thr Phe Thr Ser His Thr Pro Gly Asp His Gln Ile

100 105 110

25 Cys Leu His Ser Asn Ser Thr Arg Met Ala Leu Phe Ala Gly Gly Lys

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Leu Arg Val His Leu Asp Ile Gln Val Gly Glu His Ala Asn Asn Tyr Pro Glu Ile Ala Ala Lys Asp Lys Leu Thr Glu Leu Gln Leu Arg Ala Arg Gln Leu Leu Asp Gln Val Glu Gln Ile Gln Lys Glu Gln Asp Tyr Gln Arg Tyr Arg Glu Glu Arg Phe Arg Leu Thr Ser Glu Ser Thr Asn Gln Arg Val Leu Trp Trp Ser Ile Ala Gln Thr Val Ile Leu Ile Leu G. Thr Gly Ile Trp Gln Met Arg His Leu Lys Ser Phe Phe Glu Ala Lys Lys Leu Val <210> 92 <211> 352 <212> PRT <213> Homo sapiens <400> 92 Met Glu Ser Gly Gly Arg Pro Ser Leu Cys Gln Phe Ile Leu Leu Gly Thr Thr Ser Val Val Thr Ala Ala Leu Tyr Ser Val Tyr Arg Gln Lys

|    |     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Ala | Arg | Val | Ser | Gln | Glu | Leu | Lys | Gly | Ala | Lys | Lys | ۷al | His | Leu | Gl  |
|    |     |     | 35  |     |     |     |     | 40  |     |     |     | •   | 45  |     |     |     |
|    | Glu | Asp | Leu | Lys | Ser | Ile | Leu | Ser | Glu | Ala | Pro | Gly | Lys | Cys | Val | Pro |
| 5  |     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
|    | Tyr | Ala | Val | Ile | Glu | Gly | Ala | Val | Arg | Ser | Val | Lys | Glu | Thr | Leu | Asr |
|    | 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
|    | Ser | Gln | Phe | Val | Glu | Asn | Cys | Lys | Gly | Val | Ile | Gln | Arg | Leu | Thr | Leu |
|    |     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
| 10 | Gln | Glu | His | Lys | Met | Val | Trp | Asn | Arg | Thr | Thr | His | Leu | Trp | Asn | Asp |
|    |     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
|    | Cys | Ser | Lys | Ile | Ile | His | Gln | Arg | Thr | Asn | Thr | Val | Pro | Phe | Asp | Leu |
|    |     |     | 115 |     |     | •   |     | 120 |     |     |     |     | 125 |     |     |     |
|    | Val | Pro | His | Glu | Asp | Gly | Val | Asp | Val | Ala | Val | Arg | Val | Leu | Lys | Pro |
| 15 |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
|    | Leu | Asp | Ser | Val | Asp | Leu | Gly | Leu | Glu | Thr | Val | Tyr | Glu | Ьуs | Phe | His |
|    | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
|    | Pro | Ser | Ile | Gln | Ser | Phe | Thr | Asp | Val | Ile | Gly | His | Tyr | Ile | Ser | Gly |
|    |     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
| 20 | Glu | Arg | Pro | Lys | Gly | Ile | Gln | Glu | Thr | Glu | Glu | Met | Leu | Lys | Val | Gly |
|    |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
|    | Ala | Thr | Leu | Thr | Gly | Val | Gly | Glu | Leu | Val | Leu | Asp | Asn | Asn | Ser | Val |
|    |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
|    | Arg | Leu | Gln | Pro | Pro | Lys | Gln | Gly | Met | Gln | Tyr | Tyr | Leu | Ser | Ser | Gln |
| 25 |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |

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Asp Phe Asp Ser Leu Leu Gln Arg Gln Glu Ser Ser Val Arg Leu Trp Lys Val Leu Ala Leu Val Phe Gly Phe Ala Thr Cys Ala Thr Leu Phe Phe Ile Leu Arg Lys Gln Tyr Leu Gln Arg Gln Glu Arg Leu Arg Leu Lys Gln Met Gln Glu Glu Phe Gln Glu His Glu Ala Gln Leu Leu Ser Arg Ala Lys Pro Glu Asp Arg Glu Ser Leu Lys Ser Ala Cys Val Val Cys Leu Ser Ser Phe Lys Ser Cys Val Phe Leu Glu Cys Gly His Val Cys Ser Cys Thr Glu Cys Tyr Arg Ala Leu Pro Glu Pro Lys Lys Cys Pro Ile Cys Arg Gln Ala Ile Thr Arg Val Ile Pro Leu Tyr Asn Ser 

<210> 93

20 <211> 130

<212> PRT

<213> Homo sapiens

<400> 93

25 Met Ser Ser Ser Gly Gly Ala Pro Gly Ala Ser Ala Ser Ser Ala Pro

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Pro Ala Gln Glu Glu Met Thr Trp Trp Tyr Arg Trp Leu Cys Arg Leu Ser Gly Val Leu Gly Ala Val Ser Cys Ala Ile Ser Gly Leu Phe Asn Cys Ile Thr Ile His Pro Leu Asn Ile Ala Ala Gly Val Trp Met Met Met Ala Val Val Pro Ile Val Ile Ser Leu Thr Leu Thr Thr Leu Leu Gly Asn Ala Ile Ala Phe Ala Thr Gly Val Leu Tyr Gly Leu Ser Ala Leu Gly Lys Lys Gly Asp Ala Ile Ser Tyr Ala Arg Ile Gln Gln Gln Arg Gln Gln Ala Asp Glu Glu Lys Leu Ala Glu Thr Leu Glu Gly Glu Leu <210> 94 <211> 330 <212> PRT <213> Homo sapiens <400> 94

Met Ser Arg Cys Ala Gln Ala Ala Glu Val Ala Ala Thr Val Pro Gly

. 25

|     | 1   |     |      |     | 5   |     |       |            |     | 10    |     |       |     |     | 12  |     |
|-----|-----|-----|------|-----|-----|-----|-------|------------|-----|-------|-----|-------|-----|-----|-----|-----|
|     | Ala | Gly | Val  | Gly | Asn | Val | Gly   | Leu        | Arg | Pro   | Pro | Met   | Val | Pro | Arg | Gln |
|     |     |     |      | 20  |     |     |       |            | 25  |       |     |       |     | 30  |     |     |
|     | Ala | Ser | Phe  | Phe | Pro | Pro | Pro   | Val        | Pro | Asn   | Pro | Phe   | Val | Gln | Gln | Thr |
| 5   |     |     | 35   |     |     |     |       | 40         |     |       |     |       | 45  |     |     |     |
|     | Gln | Ile | Gly  | Ser | Ala | Arg | Arg   | Val        | Gln | Ile   | Val | Leu   | Leu | Gly | Ile | Ile |
|     |     | 50  |      |     |     |     | 55    |            |     |       |     | 60    |     |     |     |     |
|     | Leu | Leu | Pro  | Ile | Arg | Val | Leu   | Leu        | Val | Ala   | Leu | Ile   | Leu | Leu | Leu | Ala |
|     | 65  |     |      |     |     | 70  |       |            |     |       | 75  |       |     |     |     | 80  |
| 10  | Trp | Pro | Phe  | Ala | Ala | Ile | Ser   | Thr        | Val | Cys   | Cys | Pro   | Glu | Lys | Leu | Thr |
|     |     |     |      |     | 85  |     |       |            |     | 90    |     |       |     |     | 95  |     |
|     | His | Pro | Ile  | Thr | Gly | Trp | Arg   | Arg        | Lys | Ile   | Thr | Gln   | Thr | Ala | Leu | Lys |
|     |     |     |      | 100 |     |     |       |            | 105 |       |     |       |     | 110 |     |     |
|     | Phe | Leu | Gly  | Arg | Ala | Met | Phe   | Phe        | Ser | Met   | Gly | Phe   | Ile | Val | Ala | Val |
| 15  |     |     | 115  |     |     |     |       | 120        |     |       |     |       | 125 |     |     |     |
|     | Lys | Gly | Lys  | Ile | Ala | Ser | Pro   | Leu        | Glu | Ala   | Pro | Val   | Phe | Val | Ala | Ala |
|     |     | 130 |      |     |     |     | 135   |            |     |       |     | 140   |     |     |     |     |
|     | Pro | His | Ser  | Thr | Phe | Phe | Asp   | Gly        | Ile | Ala   | Cys | Val   | Val | Ala | Gly |     |
|     | 145 |     |      |     |     | 150 |       |            |     |       | 155 |       |     |     |     | 160 |
| 20  | Pro | Ser | Ile  | Val |     |     | Asn   | Glu        | Asn |       |     | Val   | Pro | Leu |     | Gly |
|     |     |     |      |     | 165 |     |       |            |     | 170   |     |       |     |     | 175 |     |
|     | Arg | Leu | Leu  |     |     | Val | . Gln | Pro        |     |       | Val | Ser   | Arg |     |     | Pro |
|     |     |     |      | 180 |     |     |       |            | 185 |       |     | _     | _   | 190 |     | 0 - |
| 25  | Asp | Ser | Arg  |     | Asn | Thr | : Ile | Asn<br>200 |     | ı Ile | Ile | . Lys | Arg |     | rnr | ser |
| / ¬ |     |     | 1 45 |     |     |     |       | 700        |     |       |     |       | ンロラ |     |     |     |

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Gly Gly Glu Trp Pro Gln Ile Leu Val Phe Pro Glu Gly Thr Cys Thr Asn Arg Ser Cys Leu Ile Thr Phe Lys Pro Gly Ala Phe Ile Pro Gly Val Pro Val Gln Pro Val Leu Leu Arg Tyr Pro Asn Lys Leu Asp Thr Val Thr Trp Thr Trp Gln Gly Tyr Thr Phe Ile Gln Leu Cys Met Leu Thr Phe Cys Gln Leu Phe Thr Lys Val Glu Val Glu Met Phe Leu Phe Phe Trp Glu Gly Ser Ser Lys His Cys Leu Lys Ile Ser Ser Phe Phe Cys Ile Phe Ser Leu Arg Arg Phe Lys Arg Arg Ile Thr Gln Arg Thr Arg Thr Ala His Leu Leu Arg Leu Ser Phe <210> 95 <211> 350 <212> PRT <213> Homo sapiens <400> 95 Met Ala Leu Pro Pro Gly Pro Ala Ala Leu Arg His Thr Leu Leu Leu · 5 

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Ala Cys Leu Val Cys Arg Lys Glu Lys Lys Thr Lys Gly Pro Ser Arg His Pro Ser Leu Ile Ser Ser Asp Ser Asn Asn Leu Lys Leu Asn Asn Val Arg Leu Pro Arg Glu Asn Met Ser Leu Pro Ser Asn Leu Gln Leu Asn Asp Leu Thr Pro Asp Ser Arg Ala Val Lys Pro Ala Asp Arg Gln Met Ala Gln Asn Asn Ser Arg Pro Glu Leu Leu Asp Pro Glu Pro Gly Gly Leu Leu Thr Ser Gln Ala Cys Leu Leu His His Gly Thr Pro Ala Leu Thr Asn Pro Trp Leu Pro His Gln Glu Gly Ala Leu Pro Gly Gly Trp Ser Pro Gln Ala His Asn Ser Thr Val Trp Lys Leu 

<210> 96

20 <211> 113

<212> PRT

<213> Homo sapiens

<400> 96

25 Met Asn Glu Thr Asn Lys Thr Leu Val Gly Pro Ser Glu Leu Pro Thr

|    | 1    |       |       |       | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
|----|------|-------|-------|-------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Ala  | Ser   | Ala   | Val   | Ala | Pro | Gly | Pro | Gly | Thr | Gly | Ala | Arg | Ala | Trp | Pro |
|    |      |       |       | 20    |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
|    | Val  | Leu   | Val   | Gly   | Phe | Val | Leu | Gly | Ala | Val | Val | Leu | Ser | Leu | Leu | Ile |
| 5  |      |       | 35    |       |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
|    | Ala  | Leu   | Ala   | Ala   | Lys | Cys | His | Leu | Cys | Arg | Arg | Tyr | His | Ala | Ser | Tyr |
|    |      | 50    |       |       |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
|    | Arg  | His   | Arg   | Pro   | Leu | Pro | Glu | Thr | Gly | Arg | Gly | Gly | Arg | Pro | Gln | Val |
|    | 65   |       |       |       |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
| 10 | Ala  | Glu   | Asp   | Glu   | Asp | Asp | Asp | Gly | Phe | Ile | Glu | Asp | Asn | Tyr | Ile | Gln |
|    |      |       |       |       | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
|    | Pro  | Gly   | Thr   | Gly   | Glu | Leu | Gly | Thr | Glu | Gly | Ser | Arg | Asp | His | Phe | Ser |
|    |      |       |       | 100   |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
|    | Leu  |       |       |       |     |     |     |     |     |     |     |     |     |     |     |     |
| 15 |      |       |       |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    |      |       |       |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <210 | )> 97 | 7     |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <21  | 1> 18 | 39    |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <212 | 2> PI | RT    |       |     |     |     |     |     |     |     |     |     |     |     |     |
| 20 | <213 | 3> Ho | omo s | sapie | ens |     |     |     |     |     |     |     |     |     |     |     |
|    |      |       |       |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <400 | 0> 9  | 7     |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | Met  | Ala   | Leu   | Leu   | Ser | Arg | Pro | Ala | Leu | Thr | Leu | Leu | Leu | Leu | Leu | Met |
|    | 1    |       |       |       | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
| 25 | Ala  | Ala   | Val   | Val   | Arg | Cys | Gln | Glu | Gln | Ala | Gln | Thr | Thr | Asp | Trp | Arg |

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|    |     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Ala | Thr | Leu | Lys | Thr | Ile | Arg | Asn | Gly | Val | His | Lys | Ile | Asp | Thr | Tyr |
|    |     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
|    | Leu | Asn | Ala | Ala | Leu | Asp | Leu | Leu | Gly | Gly | Glu | Asp | Gly | Leu | Cys | Gln |
| 5  |     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
|    | Tyr | Lys | Суѕ | Ser | Asp | Gly | Ser | Lys | Pro | Phe | Pro | Arg | Tyr | Gly | Tyr | Lys |
|    | 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
|    | Pro | Ser | Pro | Pro | Asn | Gly | Cys | Gly | Ser | Pro | Leu | Phe | Gly | Val | His | Leu |
|    |     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
| 10 | Asn | Ile | Gly | Ile | Pro | Ser | Leu | Thr | Lys | Cys | Cys | Asn | Gln | His | Asp | Arg |
|    |     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
|    | Cys | Tyr | Glu | Thr | Cys | Gly | Lys | Ser | Lys | Asn | Asp | Cys | Asp | Glu | Glu | Phe |
|    |     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
|    | Gln | Tyr | Cys | Leu | Ser | Lys | Ile | Cys | Arg | Asp | Val | Gln | Lys | Thr | Leu | Gly |
| 15 |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
|    | Leu | Thr | Gln | His | Val | Gln | Ala | Cys | Glu | Thr | Thr | Val | Glu | Leu | Leu | Phe |
|    | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
|    | Asp | Ser | Val | Ile | His | Leu | Gly | Cys | Lys | Pro | Tyr | Leu | Asp | Ser | Gln | Arg |
|    |     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
| 20 | Ala | Ala | Cys | Arg | Cys | His | Tyr | Glu | Glu | Lys | Thr | Asp | Leu |     |     |     |
|    |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     |     |     |     |
|    |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |

<210> 98

<211> 277

<212> PRT

25

# 228/346

<213> Homo sapiens

|    | _ |     | ~ ~ |
|----|---|-----|-----|
| <4 | Ð | (1) | 98  |

|    | 1400 | 0/ 5 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|----|------|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Met  | Ser  | Pro | Leu | Leu | Gly | Leu | Arg | Ser | Glu | Leu | Gln | Asp | Thr | Суѕ | Thr |
| 5  | 1    |      |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
|    | Ser  | Leu  | Gly | Leu | Met | Leu | Ser | Val | Val | Leu | Leu | Met | Gly | Leu | Ala | Arg |
|    |      |      |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
|    | Val  | Val  | Ala | Arg | Gln | Gln | Leu | His | Arg | Pro | Val | Ala | His | Ala | Phe | Val |
|    |      |      | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
| 10 | Leu  | Glu  | Phe | Leu | Ala | Thr | Phe | Gln | Leu | Cys | Суѕ | Суѕ | Thr | His | Glu | Leu |
|    |      | 50   |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
|    | Gln  | Leu  | Leu | Ser | Glu | Gln | His | Pro | Ala | His | Pro | Thr | Trp | Thr | Leu | Thr |
|    | 65   |      |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
|    | Leu  | Val  | Tyr | Phe | Phe | Ser | Leu | Val | His | Gly | Leu | Thr | Leu | Val | Gly | Thr |
| 15 |      |      |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
|    | Ser  | Ser  | Asn | Pro | Cys | Gly | Val | Met | Met | Gln | Met | Met | Leu | Gly | Gly | Met |
|    |      |      |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
|    | Ser  | Pro  | Glu | Thr | Gly | Ala | Val | Arg | Leu | Leu | Ala | Gln | Leu | Val | Ser | Ala |
|    |      | *    | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
| 20 | Leu  | Cys  | Ser | Arg | Tyr | Cys | Thr | Ser | Ala | Leu | Trp | Ser | Leu | Gly | Leu | Thr |
|    |      | 130  |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
|    | Gln  | Tyr  | His | Val | Ser | Glu | Arg | Ser | Phe | Ala | Cys | Lys | Asn | Pro | Ile | Arg |
|    | 145  |      |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
|    | Val  | Asp  | Leu | Leu | Lys | Ala | Val | Ile | Thr | Glu | Ala | Val | Cys | Ser | Phe | Leu |
| 25 |      |      |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |

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|    | Phe  | His   | Ser   | Ala  | Leu | Leu | His | Phe | Gln | Glu | Val | Arg | Thr | Lys | Leu | Arg |
|----|------|-------|-------|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    |      |       |       | 180  |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
|    | Ile  | His   | Leu   | Leu  | Ala | Ala | Leu | Ile | Thr | Phe | Leu | Val | Tyr | Ala | Gly | Gly |
|    |      |       | 195   |      |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
| 5  | Ser  | Leu   | Thr   | Gly  | Ala | Val | Phe | Asn | Pro | Ala | Leu | Ala | Leu | Ser | Leu | His |
|    |      | 210   |       |      |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
|    | Phe  | Met   | Cys   | Phe  | Asp | Glu | Ala | Phe | Pro | Gln | Phe | Phe | Ile | Val | Tyr | Trp |
|    | 225  |       |       |      |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
|    | Leu  | Ala   | Pro   | Ser  | Leu | Gly | Ile | Leu | Leu | Met | Ile | Leu | Met | Phe | Ser | Phe |
| 10 |      |       |       |      | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |
|    | Phe  | His   | Gly   | Cys  | Ile | Thr | Thr | Ile | Gln | Leu | Ile | Lys | Arg | Asn | Asn | Суз |
|    |      |       |       | 260  |     |     |     |     | 265 |     |     |     |     | 270 |     |     |
|    | Ser  | Lys   | Asp   | Ser  | Asp |     |     |     |     |     |     |     |     |     |     |     |
|    |      |       | 275   |      |     |     |     |     |     |     |     |     |     |     |     |     |
| 15 |      |       |       |      |     | •   |     |     |     |     |     |     |     |     |     |     |
|    | <210 | > 99  |       |      |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <211 | .> 27 | 74    |      |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <212 | !> PF | RT    |      |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <213 | > Ho  | omo s | apie | ens |     |     |     |     |     |     |     |     |     |     |     |
| 20 |      |       |       |      |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <400 | > 99  | )     |      |     |     |     |     |     |     |     |     |     |     |     |     |
|    | Met  | Gly   | Lys   | Ser  | Leu | Ser | His | Leu | Pro | Leu | His | Ser | Ser | Lys | Glu | Asp |
|    | 1    |       |       |      | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
|    | Ala  | Tyr   | Asp   | Gly  | Val | Thr | Ser | Glu | Asn | Met | Arg | Asn | Gly | Leu | Val | Asn |
| 25 |      |       |       | 20   |     |     |     |     | 25  |     |     |     |     | 30  |     |     |

|    | Ser | Glu | Val | His | Àsn | Glu | Asp | Gly | Arg      | Asn | Gly | Asp | Val | Ser | Gln | Phe |
|----|-----|-----|-----|-----|-----|-----|-----|-----|----------|-----|-----|-----|-----|-----|-----|-----|
|    |     |     | 35  |     |     |     |     | 40  |          |     |     |     | 45  |     |     |     |
|    | Pro | Tyr | Val | Glu | Phe | Thr | Gly | Arg | Asp      | Ser | Val | Thr | Cys | Pro | Thr | Cys |
|    | 1   | 50  |     |     |     |     | 55  |     |          | -   |     | 60  |     |     |     |     |
| 5  | Gln | Gly | Thr | Gly | Arg | Ile | Pro | Arg | Gly      | Gln | Glu | Asn | Gln | Leu | Val | Ala |
|    | 65  |     |     |     |     | 70  |     |     |          |     | 75  |     |     |     |     | 80  |
|    | Leu | Ile | Pro | Tyr | Ser | Asp | Gln | Arg | Leu      | Arg | Pro | Arg | Arg | Thr | Lys | Leu |
|    |     |     |     |     | 85  |     |     |     |          | 90  |     |     |     |     | 95  |     |
|    | Tyr | Val | Met | Ala | Ser | Val | Phe | Val | Cys      | Leu | Leu | Leu | Ser | Gly | Leu | Ala |
| 10 |     |     |     | 100 |     |     |     |     | 105      |     |     |     |     | 110 |     |     |
|    | Val | Phe | Phe | Leu | Phe | Pro | Arg | Ser | Ile      | Asp | Val | Lys | Tyr | Ile | Gly | Val |
|    |     |     | 115 |     |     |     |     | 120 |          |     |     |     | 125 |     |     |     |
|    | Lys | Ser | Ala | Tyr | Val | Ser | Tyr | Asp | Val      | Gln | Lys | Arg | Thr | Ile | Tyr | Leu |
|    |     | 130 |     |     |     |     | 135 |     |          |     |     | 140 |     |     |     |     |
| 15 | Asn | Ile | Thr | Asn | Thr | Leu | Asn | Ile | Thr      | Asn | Asn | Asn | Tyr | Tyr | Ser | Val |
|    | 145 |     |     |     |     | 150 |     |     |          |     | 155 |     |     |     |     | 160 |
|    | Glu | Val | Glu | Asn | Ile | Thr | Ala | Gln | Val<br>· | Gln | Phe | Ser | Lys | Thr | Val | Ile |
|    |     |     |     |     | 165 |     |     |     |          | 170 |     |     |     |     | 175 |     |
|    | Gly | Lys | Ala | Arg | Leu | Asn | Asn | Ile | Thr      | Ile | Ile | Gly | Pro | Leu | Asp | Met |
| 20 |     |     |     | 180 |     |     |     |     | 185      |     |     |     |     | 190 |     |     |
|    | Lys | Gln | Ile | Asp | Tyr | Thr | Val | Pro | Thr      | Val | Ile | Ala | Glu | Glu | Met | Ser |
|    |     |     | 195 |     |     |     |     | 200 |          |     |     |     | 205 |     |     |     |
|    | Tyr |     | Tyr | Asp | Phe | Cys | Thr | Leu | Ile      | Ser | Ile | Lys | Val | His | Asn | Ile |
|    |     | 210 |     |     |     |     | 215 |     |          |     |     | 220 |     |     |     |     |
| 25 | Val | Leu | Met | Met | Gln | Val | Thr | Val | Thr      | Thr | Thr | Tvr | Phe | Gly | His | Ser |

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Glu Gln Ile Ser Gln Glu Arg Tyr Gln Tyr Val Asp Cys Gly Arg Asn Thr Thr Tyr Gln Leu Gly Gln Ser Glu Tyr Leu Asn Val Leu Gln Pro Gln Gln <210> 100 <211> 390 <212> PRT <213> Homo sapiens <400> 100 Met Ile Ser Leu Pro Gly Pro Leu Val Thr Asn Leu Leu Arg Phe Leu Phe Leu Gly Leu Ser Ala Leu Ala Pro Pro Ser Arg Ala Gln Leu Gln Leu His Leu Pro Ala Asn Arg Leu Gln Ala Val Glu Gly Gly Glu Val Val Leu Pro Ala Trp Tyr Thr Leu His Gly Glu Val Ser Ser Ser Gln Pro Trp Glu Val Pro Phe Val Met Trp Phe Phe Lys Gln Lys Glu Lys Glu Asp Gln Val Leu Ser Tyr Ile Asn Gly Val Thr Thr Ser Lys Pro

|    |        |          |       |      | 85  |            |     |     |      | 90   |     |     |     |      | 95     |     |
|----|--------|----------|-------|------|-----|------------|-----|-----|------|------|-----|-----|-----|------|--------|-----|
|    | Gly    | Val      | Ser   | Leu  | Val | Tyr        | Ser | Met | Pro  | Ser  | Arg | Asn | Leu | Ser  | Leu    | Arg |
|    |        |          |       | 100  |     |            |     |     | 105  |      |     |     |     | 110  |        |     |
|    | Leu    | Glu      | Gly   | Leu  | Gln | Glu        | Lys | Asp | Ser  | Gly  | Pro | Tyr | Ser | Cys  | Ser    | Val |
| 5  |        |          | 115   |      |     |            |     | 120 |      |      |     |     | 125 |      |        |     |
|    | Asn    | Val      | Gln   | Asp  | Lys | Gln        | Gly | Lys | Ser  | Arg  | Gly | His | Ser | Ile  | Lys    | Thr |
|    |        | 130      |       |      |     |            | 135 |     |      |      |     | 140 |     |      |        |     |
|    | Leu    | Glu      | Leu   | Asn  | Val | Leu        | Val | Pro | Pro  | Ala  | Pro | Pro | Ser | Cys  | Arg    | Leu |
|    | 145    |          |       |      |     | 150        |     |     |      |      | 155 |     |     |      |        | 160 |
| LO | Gln    | Gly      | Val   | Pro  | His | Val        | Gly | Ala | Asn  | Val  | Thr | Leu | Ser | Cys  | Gln    | Ser |
|    |        |          |       |      | 165 |            |     |     |      | 170  |     |     |     |      | 175    |     |
|    | Pro    | Arg      | Ser   | Lys  | Pro | Ala        | ۷al | Gln | Tyr  | Gln  | Trp | Asp | Arg | Gln  | Leu    | Pro |
|    |        |          |       | 180  |     |            |     |     | 185  |      |     |     |     | 190  |        |     |
|    | Ser    | Phe      | Gln   | Thr  | Phe | Phe        | Ala | Pro | Ala  | Leu  | Asp | Val | Ile |      | Glv    | Ser |
| L5 |        |          | 195   |      |     |            |     | 200 |      |      | -   |     | 205 | •    | -      |     |
|    | Leu    | Ser      | Leu   | Thr  | Asn | Leu        | Ser | Ser | Ser  | Met  | Ala | Glv |     | Tvr  | Val    | Cvs |
|    |        | 210      |       |      |     |            | 215 |     |      |      |     | 220 |     | -3   |        | -2- |
|    | Lvs    |          | His   | Asn  | Glu | Val        |     | Thr | Ala  | Gln  | Cvs |     | Val | Thr  | T.e.11 | Glu |
|    | 225    |          |       |      |     | 230        | 023 |     | 1114 | OIII | 235 | non | Val | 1111 | Deu    | 240 |
| 20 |        | Sor      | ሞኮድ   | G) w | Pro | Gly        | מות | 71- | Wal  | ซอโ  |     | C1  | 71- | ***  | 77-1   |     |
| -0 | Val    | DCI      | 1111  | GIĀ  |     | GLY        | ма  | ALA | val  |      | ATG | GIY | ATa | Val  |        | GTÀ |
|    | Mla sa | <b>7</b> | *7- 7 | 01   | 245 | <b>~</b> 1 | _   |     |      | 250  | _   | •   | _   | _    | 255    |     |
|    | Tnr    | Leu      | val   |      | Leu | Gly        | Leu | Leu |      | Gly  | Leu | Val | Leu |      | Tyr    | His |
|    |        |          |       | 260  |     |            |     |     | 265  |      |     |     |     | 270  |        |     |
|    | Cys    | Arg      |       | Lys  | Ala | Leu        | Glu | Glu | Pro  | .Ala | Asn | Asp | Ile | Lys  | Glu    | Asp |
| 25 |        |          | 275   |      |     |            |     | 280 |      |      |     |     | 285 |      |        |     |

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Ala Ile Ala Pro Arg Thr Leu Pro Trp Pro Lys Ser Ser Asp Thr Ile 290 295 300 Ser Lys Asn Gly Thr Leu Ser Ser Val Thr Ser Ala Arg Ala Leu Arg 305 310 315 320 5 Pro Pro His Gly Pro Pro Arg Pro Gly Ala Leu Thr Pro Thr Pro Ser 325 330 335 Leu Ser Ser Gln Ala Leu Pro Ser Pro Arg Leu Pro Thr Thr Asp Gly 340 345 350 Ala His Pro Gln Pro Ile Ser Pro Ile Pro Gly Gly Val Ser Ser Ser 10 355 360 365 Gly Leu Ser Arg Met Gly Ala Val Pro Val Met Val Pro Ala Gln Ser 370 375 380 Gln Ala Gly Ser Leu Val 385 390 15 <210> 101 <211> 684 <212> DNA <213> Homo sapiens 20 <400> 101 atggcaggtg tcggggctgg gcctctgcgg gcgatggggc ggcaggccct gctgcttctc 60 gcgctgtgcg ccacaggcgc ccaggggctc tacttccaca tcggcgagac cgagaagcgc 120 tgtttcatcg aggaaatccc cgacgagacc atggtcatcg gcaactatcg tacccagatg 180 25

tgggataagc agaaggaggt cttcctgccc tcgacccctg gcctgggcat gcacgtggaa 240

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acgttcacct cccacacgce cggtgaccat caaatctgte tgcactccaa ttctaccagg 360
atggctctct tcgctggtgg caaactgcgg gtgcatctcg acatccaggt tggggagcat 420
gccaacaact accctgagat tgctgcaaaa gataagctga cggagctaca gctccgcgcc 480
cgccagttgc ttgatcaggt ggaacagatt cagaaggagc aggattacca aaggtatcgt 540
gaagagcgct tccgactgac gagcgagagc accaaccaga gggtcctatg gtggtccatt 600
gctcagactg tcatcctcat cctcactggc atctggcaga tgcgtcacct caagagcttc 660
tttgaggcca agaagctggt gtag 684

10 <210> 102

5

<211> 1059

<212> DNA

<213> Homo sapiens

15 <400> 102

20

25

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ctggtcctgg acaacaacte tgtccgcctg cagccgcca aacaaggcat gcagtactat 660 ctaagcagcc aggacttcga cagcctgctg cagaggcagg agtcgagcgt caggctctgg 720 aaggtgctgg cgctggtttt tggctttgcc acatgtgcca ccctcttctt cattctccgg 780 aagcagtatc tgcagcggca ggagcgcctg cgcctcaagc agatgcagga ggagttccag 840 gagcatgagg cccagctgct gagccgagcc aagcctgagg acagggagag tctgaagagc 900 gcctgtgtag tgtgtctgag cagcttcaag tcctgcgtct ttctggagtg tgggcacgtt 960 tgttcctgca ccgagtgcta ccgcgccttg ccagagccca agaagtgccc tatctgcaga 1020 caggcgatca cccgggtgat acccctgtac aacagctaa

10 <210> 103

5

<211> 393

<212> DNA

<213> Homo sapiens

15 <400> 103

20

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<210> 104

25 <211> 993

#### 236/346

<212> DNA

<213> Homo sapiens

<400> 104

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<210> 105

<211> 1053

25 <212> DNA

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<213> Homo sapiens

<400> 105

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<210> 106

<211> 342

25 <212> DNA

### 238/346

<213> Homo sapiens

<400> 106

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10

5

<210> 107

<211> 570

<212> DNA

<213> Homo sapiens

15

20

25

<400> 107

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ggcgttcata agatagacae gtacctgaae geegeettgg accteetggg aggegaggae 180
ggtetetgec agtataaatg cagtgacgga tetaageett teecacgtta tggttataaa 240
ecetececae egaatggatg tggeteteca etgtttggtg tteatettaa eattggtate 300
eetteeetga caaagtgttg caaccaacae gacaggtget atgaaacetg tggeaaaage 360
aagaatgaet gtgatgaaga attecagtat tgeeteteca agatetgeeg agatgtacag 420
aaaacactag gactaactea geatgtteag geatgtgaaa caacagtgga getettgttt 480
gacagtgtta tacatttagg ttgtaaacca tatetggaca gecaacgage egeatgeagg 540

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<210> 108

<211> 834

5 <212> DNA

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15

20

<213> Homo sapiens

<400> 108

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aggeeggtgg cecaegeett egteetggag tttetageea cetteeaget etgetgetge 180
acceaegage tgeaactget gagegaacag caceeegege acceeacetg gaegetgaeg 240
etegtetaet tetteteget tgtgeatgge etgaetetgg tgggeaegte cageaaceeg 300
tgeggegtga tgatgeagat gatgetgggg ggeatgteee eegagaeggg tgeggtgagg 360
etattggete agetggttag tgeeetgtge ageaggtaet geacaagege ettgtggage 420
ttgggtetga eccagtatea egteagegag aggagetteg ettgeaagaa teceateega 480
gtegaettge teaaageggt eateacagag geegtetget eettetett eeacageget 540
etgetgeaet teeaggaagt eegaaceaag ettegtatee acetgetgge tgeaeteate 600
acettttgg tetatgeagg aggaagteta acaggagetg tatttaatee agetttggea 660
etttegetae attteatgtg ttttgatgaa geatteeete agtttttat agtataetgg 720
etggeteett etttaggtat attgttgatg attttgatgt teagetttt ceatggetge 780
ataacaacea tacaattaat aaaaaggaat aactgtteea aagaeteaga etaa 834

<210> 109

25 <211> 825

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<212> DNA

<213> Homo sapiens

<400> 109

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<211> 1173

<212> DNA

<213> Homo sapiens

25 <400> 110

## 241/346

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|------------|------------|------------|------------|------------|------------|------|
| agtgccctcg | cgccccctc  | gcgggcccag | ctgcaactgc | acttgcccgc | caaccggttg | 120  |
| caggcggtgg | agggagggga | agtggtgctt | ccagcgtggt | acaccttgca | cggggaggtg | 180  |
| tcttcatccc | agccatggga | ggtgcccttt | gtgatgtggt | tcttcaaaca | gaaagaaaag | 240  |
| gaggatcagg | tgttgtccta | catcaatggg | gtcacaacaa | gcaaacctgg | agtatccttg | 300  |
| gtctactcca | tgccctcccg | gaacctgtcc | ctgcggctgg | agggtctcca | ggagaaagac | 360  |
| tctggcccct | acagctgctc | cgtgaatgtg | caagacaaac | aaggcaaatc | taggggccac | 420  |
| agcatcaaaa | ccttagaact | caatgtactg | gttcctccag | ctcctccatc | ctgccgtctc | 480  |
| cagggtgtgc | cccatgtggg | ggcaaacgtg | accctgagct | gccagtctcc | aaggagtaag | 540  |
| cccgctgtcc | aataccagtg | ggatcggcag | cttccatcct | tccagacttt | ctttgcacca | 600  |
| gcattagatg | tcatccgtgg | gtctttaagc | ctcaccaacc | tttcgtcttc | catggctgga | 660  |
| gtctatgtct | gcaaggccca | caatgaggtg | ggcactgccc | aatgtaatgt | gacgctggaa | 720  |
| gtgagcacag | ggcctggagc | tgcagtggtt | gctggagctg | ttgtgggtac | cctggttgga | 780  |
| ctggggttgc | tggctgggct | ggtcctcttg | taccactgcc | ggggcaaggc | cctggaggag | 840  |
| ccagccaatg | atatcaagga | ggatgccatt | gctccccgga | ccctgccctg | gcccaagagc | 900  |
| tcagacacaa | tctccaagaa | tgggaccctt | tcctctgtca | cctccgcacg | agccctccgg | 960  |
| ccaccccatg | gccctcccag | gcctggtgca | ttgaccccca | cgcccagtct | ctccagccag | 1020 |
| gccctgccct | caccaagact | gcccacgaca | gatggggccc | accctcaacc | aatatcccc  | 1080 |
| atccctggtg | gggtttcttc | ctctggcttg | agccgcatgg | gtgctgtgcc | tgtgatggtg | 1140 |
| cctgcccaga | gtcaagctgg | ctctctggta | tga        |            |            | 1173 |

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<210> 111

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<211> 1894

<212> DNA

25 <213> Homo sapiens

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|    | <22  | 1> C  | DS    |       |       |      |      |      |      |       |       |     |     |       |       |     |     |
|    | <22  | 2> (  | 36).  | . (71 | 9)    |      |      |      |      |       |       |     |     |       |       |     |     |
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|    | <400 | 0> 1: | 1,1   |       |       |      |      |      |      |       |       |     |     |       |       |     |     |
|    | gcaa | aatg  | tgc ( | gcag  | geget | tt a | gggg | ctga | g gc | gcg a | atg   | gca | ggt | gtc   | ggg   | gct | 53  |
|    |      |       |       |       |       |      |      |      |      | 1     | Met . | Ala | Gly | Val ( | Gly . | Ala |     |
|    |      |       |       |       |       |      |      |      |      |       | 1     |     |     |       | 5     |     |     |
| 10 | ggg  | cct   | ctg   | cgg   | gcg   | atg  | ggg  | cgg  | cag  | gcc   | ctg   | ctg | ctt | ctc   | gcg   | ctg | 101 |
|    | Gly  | Pro   | Leu   | Arg   | Ala   | Met  | Gly  | Arg  | Gln  | Ala   | Leu   | Leu | Leu | Leu   | Ala   | Leu |     |
|    |      |       |       | 10    |       |      |      |      | 15   |       |       |     |     | 20    |       |     |     |
|    | tgc  | gcc   | aca   | ggc   | gcc   | cag  | ggg  | ctc  | tac  | ttc   | cac   | atc | ggc | gag   | acc   | gag | 149 |
| -  | Cys  | Ala   | Thr   | Gly   | Ala   | Gln  | Gly  | Leu  | Tyr  | Phe   | His   | Ile | Gly | Glu   | Thr   | Glu |     |
| 15 | •    |       | 25    |       |       |      |      | 30   |      |       |       |     | 35  |       |       |     |     |
|    | aag  | cgc   | tgt   | ttc   | atc   | gag  | gaa  | atc  | ccc  | gac   | gag   | acc | atg | gtc   | atc   | ggc | 197 |
|    | Lys  | Arg   | Cys   | Phe   | Ile   | Glu  | Glu  | Ile  | Pro  | Asp   | Glu   | Thr | Met | Val   | Ile   | Gly |     |
|    |      | 40    |       |       |       |      | 45   |      |      |       |       | 50  |     |       |       |     |     |
|    | aac  | tat   | cgt   | acc   | cag   | atg  | tgg  | gat  | aag  | cag   | aag   | gag | gtc | ttc   | ctg   | ccc | 245 |
| 20 | Asn  | Tyr   | Arg   | Thr   | Gln   | Met  | Trp  | Asp  | Lys  | Gln   | Lys   | Glu | Val | Phe   | Leu   | Pro |     |
|    | 55   |       |       |       |       | 60   |      |      |      |       | 65    |     |     |       |       | 70  |     |
|    | tcg  | acc   | cct   | ggc   | ctg   | ggc  | atg  | cac  | gtg  | gaa   | gtg   | aag | gac | ccc   | gac   | ggc | 293 |
|    | Ser  | Thr   | Pro   | Gly   | Leu   | Gly  | Met  | His  | Val  | Glu   | Val   | Lys | Asp | Pro   | Asp   | Gly |     |
|    |      |       |       |       | 75    |      |      |      |      | 80    |       |     |     |       | 85    |     |     |
| 25 | aag  | gtg   | gtg   | ctg   | tcc   | cgg  | cag  | tac  | ggc  | tcg   | gag   | ggc | cgc | ttc   | acg   | ttc | 341 |

|    | Lys Val Val | l Leu Ser Arg | Gln Tyr Gl  | y Ser Glu Gly | Arg Phe T  | nr Phe     |
|----|-------------|---------------|-------------|---------------|------------|------------|
|    |             | 90            | 9           | 5             | 100        |            |
|    | acc tcc cad | c acg ccc ggt | gac cat ca  | a atc tgt ctg | cac tcc as | at tct 389 |
|    | Thr Ser His | s Thr Pro Gly | Asp His Gl  | n Ile Cys Leu | His Ser As | sn Ser     |
| 5  | 105         | 5             | 110         |               | 115        |            |
|    | acc agg ato | g gct ctc ttc | gct ggt gg  | c aaa ctg cgg | gtg cat c  | tc gac 437 |
|    | Thr Arg Met | t Ala Leu Phe | Ala Gly Gl  | y Lys Leu Arg | Val His Le | eu Asp     |
|    | 120         |               | 125         | 130           |            |            |
|    | atc cag gtt | t ggg gag cat | gcc aac aa  | c tac cct gag | att gct g  | ca aaa 485 |
| 10 | Ile Gln Val | l Gly Glu His | Ala Asn As  | n Tyr Pro Glu | Ile Ala Al | la Lys     |
|    | 135         | 140           |             | 145           |            | 150        |
|    | gat aag cto | g acg gag cta | cag ctc cg  | c gcc cgc cag | ttg ctt ga | at cag 533 |
|    | Asp Lys Leu | ı Thr Glu Leu | Gln Leu Ar  | g Ala Arg Gln | Leu Leu As | sp Gln     |
|    |             | 155           |             | 160           | 16         | 55         |
| 15 | gtg gaa cag | g att cag aag | gag cag ga  | t tac caa agg | tat cgt ga | aa gag 581 |
|    | Val Glu Glr | n Ile Gln Lys | Glu Gln As  | p Tyr Gln Arg | Tyr Arg G  | lu Glu     |
|    |             | 170           | 17          | 5             | 180        |            |
|    | cgc ttc cga | a ctg acg agc | gag agc ac  | c aac cag agg | gtc cta to | gg tgg 629 |
|    | Arg Phe Arg | g Leu Thr Ser | Glu Ser Th  | r Asn Gln Arg | Val Leu Tr | p Trp      |
| 20 | 185         | 5             | 190         |               | 195        |            |
|    | tcc att gct | cag act gtc   | atc ctc at  | c ctc act ggc | atc tgg ca | ng atg 677 |
|    | Ser Ile Ala | a Gln Thr Val | Ile Leu Il  | e Leu Thr Gly | Ile Trp Gl | n Met      |
|    | 200         |               | 205         | 210           |            |            |
|    | cgt cac ctc | aag agc ttc   | ttt gag gc  | c aag aag ctg | gtg tag    | 719        |
| 25 | Arg His Lev | Lys Ser Phe   | Phe Glu Ala | a Lys Lys Leu | Val        |            |

#### 244/346

215 220 225

tgccctcttt gtatgaccct tcctttttac ctcatttatt tggtactttc cccacacagt 779 cctttatcca cctggatttt tagggaaaaa aatgaaaaag aataagtcac attggttcca 839 tggccacaaa ccattcagat cagccacttg ctgaccctgg ttcttaagga cacatgacat 899 tagtccaatc tttcaaaatc ttgtcttagg gcttgtgagg aatcagaact aacccaggac 959 tcaqtcctqc ttcttttqcc tcqaqtqatt ttcctctqtt tttcactaaa taaqcaaatq 1019 aaaactctct ccattacctt ctgctttctc tttgtccact tacgcagtag gtgactggca 1079 tgtgccacag agcaggccct gcctcactgt ctgctggtca gttctgggtt cacttaatgg 1139 ctttgtgaat gtaaataagg ggcaggtctt ggccctagag gattgagatg tttttctaaa 1199 tettagaact attitiggat aaattatata titteettee tagtagaagt gitaetgeet 1259 ttttttttt ttttttgag ttttgctctt gtcgcccagg ctggagtgca atggcgtgat 1379 ctcageteac tggcaacate tgectecegg gttcaaatga ttetcetgee tcagteteet 1439 gagtagctgg gattacaggt gcccgccacc acgctcagct aatttttgta tttttagtag 1499 agatggggtt ttaccatgtt ggccaggctg gtcttagact cctgacctca gttgatccac 1559 . ctgcctcagc ctctgcattc agtttattca catatttttg gtaactccca tggcagctcc 1619 taggatttca gcggtctgtg ggccagaaag caggcaccag ggctgacctc aaggccgtat 1679 cagagggcca agcagagttc ttttggatac ctgcttttca tcccacaggg ccttagagtc 1739 agaggtaagg tagcaacaga gctagaatgg ggcaatgcac tcttaccctc cttctcaact 1799 tttatttaag ctgtgctaaa tgttttcttc aagggaacca gatttagttc tttacagaat 1859 tttccagtga aataaactct catgttattg ttccc 1894

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<211> 2413

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245/346

<213> Homo sapiens

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<400> 112

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. 10 Met

1

gag agc gga ggg cgg ccc tcg ctg tgc cag ttc atc ctc ctg ggc acc 165 Glu Ser Gly Gly Arg Pro Ser Leu Cys Gln Phe Ile Leu Leu Gly Thr

5 10 15

acc tct gtg gtc acc gcc gcc ctg tac tcc gtg tac cgg cag aag gcc 213

Thr Ser Val Val Thr Ala Ala Leu Tyr Ser Val Tyr Arg Gln Lys Ala

20 25 30

cgg gtc tcc caa gag ctc aag gga gct aaa aaa gtt cat ttg ggt gaa 261
Arg Val Ser Gln Glu Leu Lys Gly Ala Lys Lys Val His Leu Gly Glu

20 35 40 45

gat tta aag agt att ctt tca gaa gct cca gga aaa tgc gtg cct tat 309
Asp Leu Lys Ser Ile Leu Ser Glu Ala Pro Gly Lys Cys Val Pro Tyr

50 55 60 65

gct gtt ata gaa gga gct gtg cgg tct gtt aaa gaa acg ctt aac agc 357 . 25 Ala Val Ile Glu Gly Ala Val Arg Ser Val Lys Glu Thr Leu Asn Ser

|    |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |     |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | cag | ttt | gtg | gaa | aac | tgc | aag | ggg | gta | att | cag | cgg | ctg | aca | ctt | cag | 405 |
|    | Gln | Phe | Val | Glu | Asn | Cys | Lys | Gly | Val | Ile | Gln | Arg | Leu | Thr | Leu | Gln |     |
|    |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |     |     |
| 5  | gag | cac | aag | atg | gtg | tgg | aat | cga | acc | acc | cac | ctt | tgg | aat | gat | tgc | 453 |
|    | Glu | His | Lys | Met | Val | Trp | Asn | Arg | Thr | Thr | His | Leu | Trp | Asn | Asp | Cys | .)  |
|    |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |     |     |
|    | tca | aag | atc | att | cat | cag | agg | acc | aac | aca | gtg | ccc | ttt | gac | ctg | gtg | 501 |
|    | Ser | Lys | Ile | Ile | His | Gln | Arg | Thr | Asn | Thr | Val | Pro | Phe | Asp | Leu | Val |     |
| LO |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |     |     |
|    | ccc | cac | gag | gat | ggc | gtg | gat | gtg | gct | gtg | cga | gtg | ctg | aag | ccc | ctg | 549 |
|    | Pro | His | Glu | Asp | Gly | Val | Asp | Val | Ala | Val | Arg | Val | Leu | Lys | Pro | Leu |     |
|    | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     | 145 |     |
| •  | gac | tca | gtg | gat | ctg | ggt | cta | gag | act | gtg | tat | gag | aag | ttc | cac | ccc | 597 |
| L5 | Asp | Ser | Val | Asp | Leu | Gly | Leu | Glu | Thr | Val | Tyr | Glu | Lys | Phe | His | Pro |     |
|    |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |     |     |
|    | tcg | att | cag | tcc | ttc | acc | gat | gtc | atc | ggc | cac | tac | atc | agc | ggt | gag | 645 |
|    | Ser | Ile | Gln | Ser | Phe | Thr | Asp | Val | Ile | Gly | His | Tyr | Ile | Ser | Gly | Glu |     |
|    |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |     |     |
| 20 | cgg | ccc | aaa | ggc | atc | caa | gag | acc | gag | gag | atg | ctg | aag | gtg | ggg | gcc | 693 |
|    | Arg | Pro | Lys | Gly | Ile | Gln | Glu | Thr | Glu | Glu | Met | Leu | Lys | Val | Gly | Ala |     |
|    |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     | •   |     |
|    | acc | ctc | aca | ggg | gtt | ggc | gaa | ctg | gtc | ctg | gac | aac | aac | tct | gtc | cgc | 741 |
|    | Thr | Leu | Thr | Gly | Val | Gly | Glu | Leu | Val | Leu | Asp | Asn | Asn | Ser | Val | Arg |     |
| 25 |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |     |     |

## 247/346

|    | ctg | cag | ccg | CCC | aaa | caa | ggc | atg | cag | tac | tat | cta | agc | agc | cag | gac | 789  |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|    | Leu | Gln | Pro | Pro | Lys | Gln | Gly | Met | Gln | Tyr | Tyr | Leu | Ser | Ser | Gln | Asp |      |
|    | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     | 225 |      |
|    | ttc | gac | agc | ctg | ctg | cag | agg | cag | gag | tcg | agc | gtc | agg | ctc | tgg | aag | 837  |
| 5  | Phe | Asp | Ser | Leu | Leu | Gln | Arg | Gln | Glu | Ser | Ser | Val | Arg | Leu | Trp | Lys |      |
|    |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |     |      |
|    | gtg | ctg | gcg | ctg | gtt | ttt | ggc | ttt | gcc | aca | tgt | gcc | acc | ctc | ttc | ttc | 885  |
|    | Val | Leu | Ala | Leu | Val | Phe | Gly | Phe | Ala | Thr | Cys | Ala | Thr | Leu | Phe | Phe |      |
|    |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |     |      |
| 10 | att | ctc | cgg | aag | cag | tat | ctg | cag | cgg | cag | gag | cgc | ctg | cgc | ctc | aag | 933  |
|    | Ile | Leu | Arg | Lys | Gln | Tyr | Leu | Gln | Arg | Gln | Glu | Arg | Leu | Arg | Leu | Lys |      |
|    |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |     |      |
|    | cag | atg | cag | gag | gag | ttc | cag | gag | cat | gag | gcc | cag | ctg | ctg | agc | cga | 981  |
|    | Gln | Met | Gln | Glu | Glu | Phe | Gln | Glu | His | Glu | Ala | Gln | Leu | Leu | Ser | Arg |      |
| 15 |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |     |      |
|    | gcc | aag | cct | gag | gac | agg | gag | agt | ctg | aag | agc | gcc | tgt | gta | gtg | tgt | 1029 |
|    | Ala | Lys | Pro | Glu | Asp | Arg | Glu | Ser | Leu | Lys | Ser | Ala | Cys | Val | Val | Cys |      |
|    | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     | 305 |      |
|    | ctg | agc | agc | ttc | aag | tcc | tgc | gtc | ttt | ctg | gag | tgt | ggg | cac | gtt | tgt | 1077 |
| 20 | Leu | Ser | Ser | Phe | Lys | Ser | Cys | Val | Phe | Leu | Glu | Cys | Gly | His | Val | Cys |      |
|    |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |     |      |
|    | tcc | tgc | acc | gag | tgc | tac | cgc | gcc | ttg | cca | gag | ccc | aag | aag | tgc | cct | 1125 |
|    | Ser | Cys | Thr | Glu | Cys | Tyr | Arg | Ala | Leu | Pro | Glu | Pro | Lys | Lys | Cys | Pro |      |
|    |     |     |     | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |     |      |
| 25 | atc | tgc | aga | cag | gcg | atc | acc | cgg | gtg | ata | ccc | ctg | tac | aac | agc | taa | 1173 |

9

#### 248/346

Ile Cys Arg Gln Ala Ile Thr Arg Val Ile Pro Leu Tyr Asn Ser

340 345 350

tagtttggaa gccgcacagc ttgacctgga agcacccctg ccccttttc agggattttt 1233 atctcgaggc ctttggagga gcagtggtgg gggtagctgt cacctccagg tatgattgag 1293 ggaggaattg ggtagaaact ctccagaccc atgcctccaa tggcaggatg ctgcctttcc 1353 cacctgagag gggaccctgt ccatgtgcag cctcatcaga gcctcaccct gggaggatgc 1413 cgtggcgtct cctcccagga gccagatcag tgcgagtgtg actgaaaatg cctcatcact 1473 taagcaccaa agccagtgat cagcagctct tctgttcctg tgtcttctgt ttttttctgg 1533 tgaatcgttg cttgctgtgg acttggtgga ggactcagag gggaggaaag gctgggccc 1593 gagtacaacg gatgccttgg gtgctgcctc cgaagaqact ctqccqcaqc ttttcttctt 1653 tttcctcatg ccccgggaaa cagtctttct tcagaattgt caggctgggc aggtcaactt 1713 gtgttccttt cccctcacct gcttgcctcc ttaacgcctg cacgtgtgtg tagaggacaa 1773 aagaaagtga agtcagcaca tccgcttctg cccagatggt tggggccccg ggcaacagat 1833 tgaagagaga tcatgtgaag ggcagttggt caggcaggcc tcctggtttc gccactggcc 1893 ctgatttgaa ctcctgccac ttgggagagc tcggggtggt ccctggtttt ccctcctgga 1953 gaatgaggeg cagaggeete geeteetgaa ggacqeaqtq tqqatqeeac tqqeetaqtq 2013 tectggeete acagetteet tgcaaggetg teacaaggaa aagcageegg etggeaceet 2073 gagcatatgc cctcttgggg ctccctcatc cagcccgtcg cagctttgac atcttggtgt 2133 acteatgteg etteteettg tgttaceece teecagtatt accatttgee ecteacetge 2193 ccttggtgag ccttttagtg caagacagat ggggctgttt tcccccacct ctgagtagtt 2253 ggaggtcaca tacacagete ttttttatt geeettttet geetetgaat gtteatetet 2313 cgtcctcctt tgtgcaggcg aggaaggggt gccctcaggg qccqacacta gtatgatqca 2373 gtgtccagtg tgaacagcag aaattaaaca tgttgcaacc 2413

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249/346

<211> 2376

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<213> Homo sapiens

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<400> 113

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Met Ser Ser Ser Gly Gly Ala

L 5

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Pro Gly Ala Ser Ala Ser Ser Ala Pro Pro Ala Gln Glu Glu Gly Met

15 10 15 20

60

acg tgg tgg tac cgc tgg ctg tgt cgc ctg tct ggg gtg ctg ggg gca 151
Thr Trp Trp Tyr Arg Trp Leu Cys Arg Leu Ser Gly Val Leu Gly Ala

25 30 35

gtc tct tgc gcg atc tct ggc ctc ttc aac tgc atc acc atc cac cct 199

Val Ser Cys Ala Ile Ser Gly Leu Phe Asn Cys Ile Thr Ile His Pro
40 45 50 55

ctg aac atc gcg gcc ggc gtg tgg atg atg atg gcg gtc gtt ccc atc 247
Leu Asn Ile Ala Ala Gly Val Trp Met Met Ala Val Val Pro Ile

65 70

gtc atc agc ctg acc ctg acc acg ctg ctg ggc aac gcc atc gcc ttt 295

|     | Val  | Ile   | Ser | Leu   | Thr   | Leu   | Thr  | Thr   | Leu   | Leu   | Gly   | Asn  | Ala   | Ile         | Ala  | Phe    |     |
|-----|------|-------|-----|-------|-------|-------|------|-------|-------|-------|-------|------|-------|-------------|------|--------|-----|
|     |      |       |     | 75    |       |       |      |       | 80    |       |       |      |       | 85          |      |        |     |
|     | gct  | acg   | ggg | gtg   | ctg   | tac   | gga  | ctc   | tct   | gct   | ctg   | ggc  | aaa   | aag         | ggc  | gat    | 343 |
|     | Ala  | Thr   | Gly | Val   | Leu   | Tyr   | Gly  | Leu   | Ser   | Ala   | Leu   | Gly  | Lys   | Lys         | Gly  | Asp    |     |
| 5   |      |       | 90  |       |       |       |      | 95    |       |       |       |      | 100   |             |      |        |     |
|     | gcg  | atc   | tcc | tat   | gcc   | agg   | atc  | cag   | cag   | cag   | agg   | cag  | cag   | gcg         | gat  | gag    | 391 |
|     | Ala  | Ile   | Ser | Tyr   | Ala   | Arg   | Ile  | Gln   | Gln   | Gln   | Arg   | Gln  | Gln   | Ala         | Asp  | Glu    |     |
|     |      | 105   |     |       |       |       | 110  |       |       |       |       | 115  |       |             |      |        |     |
|     | gag  | aag   | ctc | gcg   | gag   | acc   | ctg  | gag   | ggg   | gag   | ctg   | tga  | agg   | gctg        | ggc  |        | 437 |
| 10  | Glu  | Lys   | Leu | Ala   | Glu   | Thr   | Leu  | Glu   | Gly   | Glu   | Leu   |      |       |             |      |        |     |
|     | 120  |       |     |       |       | 125   |      |       |       |       | 130   |      |       |             |      |        |     |
|     | gcc  | cctc  | cct | ccct  | gtcc  | cc to | cttc | tggct | t cto | gtgt  | gggt  | cca  | agtg  | agg         | cctg | gactgt | 497 |
|     | ccad | cgcto | gag | gcac  | agcct | tg ga | agag | gggc  | c ttt | gca   | cgtg  | tcc  | ctaca | acc         | tgga | gtcctc | 557 |
|     | tgcl | cct   | ttc | tcca  | gact  | gg ct | ttaa | gcca  | g gag | gcca  | ctgg  | ctg  | ctggi | tgt         | gagg | gtctgg | 617 |
| 15  | gct  | gctg  | gac | ttga  | ggca  | ga go | cctg | cagca | a gct | tgtgi | tgga  | cact | tacc  | cag         | ccct | actcct | 677 |
|     | ctg  | ctgg  | gtg | ggtc  | tgcaq | ga to | ctca | cacca | a caq | gaca  | gggc  | tgc  | ctgt  | gac         | ctgc | tgtgac | 737 |
|     | ctg  | ggago | cag | cttc  | cct   | gg aq | gatg | ctggi | cct   | egget | ttga  | ggg  | gagg  | ggc         | aagt | gggacc | 797 |
|     | ctg  | ccac  | ctg | ggca  | ctga  | gc aq | gagg | gacci | t cc  | cca   | gctc  | tct  | tagc  | agg         | tgga | gcccca | 857 |
|     | gggd | cctg  | gga | cagc  | ctgc  | eg et | tgcc | agcaa | a cci | ccca  | actg  | ctg  | ccta  | <b>3</b> 33 | tgca | gcgccc | 917 |
| 20  | acto | gtca  | ccc | tgcci | ttct  | ga aq | gaag | ccca  | c ag  | ggct  | ccta  | agg  | tgca  | ccc         | cggt | acctgg | 977 |
|     | aact | tgca  | gcc | ttgg  | cagt  | ga ci | tgga | cagci | t ggg | gtgg  | ggga  | tgc  | tccc  | tgc         | tggc | cctggg | 103 |
|     |      |       |     |       |       |       |      |       |       |       |       |      |       |             |      | ctgggg |     |
|     |      |       |     |       |       |       |      |       |       |       |       |      |       |             |      | ctcagg |     |
| 0.5 |      |       |     |       |       |       |      |       |       |       |       |      |       |             |      | gctgtc |     |
| 25  | CCC  | acta  |     | tagg  | tacc  | 24 44 | ctat | ~~~~  | . ~~  | 2200  | ant a | 000  | ~~~   | ~~~         | atro | 2020   | 127 |

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|    | ctggtgccca | ggatgtgcac | ccccatattc | cctctgccct | gtggcctcag | cccgctggcc | 1337 |
|----|------------|------------|------------|------------|------------|------------|------|
|    | tctctgaccg | tgaggctggc | tctcagccat | cgggcaggtg | cctggtcggg | cctggcttag | 1397 |
|    | cccaggtggg | gcttggcaga | agcgggcggg | tgtggaagat | attccatctg | gggccaaccc | 1457 |
|    | caggctgggc | ctgcgctgag | cttctggagc | gcaggtactg | ggtcttgcta | agtgaactgt | 1517 |
| 5  | ttcccaggaa | cacctctcgg | gcccatctgc | gtctgaggct | gggagtggca | tctgaggccg | 1577 |
|    | ggagtggcat | ctgaggccag | gagtggcagg | ctggtgggct | gggcgtgggg | ttttctgggc | 1637 |
|    | cctgcccagt | actgccctgg | ggacttggtg | ggctcctggg | tcagcagcat | cccacccctg | 1697 |
|    | ggagtctggc | cagctgagcc | ccagggtggc | aggggcatta | tagcctggtg | gacatgtgcc | 1757 |
|    | ttcagggttc | ctccggggcc | accttcctca | ggccagtgct | gggttcaaag | ggctgtgtgt | 1817 |
| 10 | gtgtgtgtgt | gtgtgtgtgt | gtatgtatat | gtgtgtgggt | gcacacatct | gtcccatgta | 1877 |
|    | tgcagtgaga | cctgtctacc | tcccacaagg | agcaagggct | ctgcccgccc | tctgctcatt | 1937 |
|    | cctacccagg | tagtgggacc | ccgggccccc | ttctgcctgg | cttgcctgct | tctgcccttt | 1997 |
|    | ccagaggggt | ctcactgaca | gccagagaca | gcaggagaag | ggttggctgt | ggatcaagga | 2057 |
|    | aggctgcccc | tgtaccctgt | ggggaaatgg | tgggtgcatg | gctggatgca | gaggtggaag | 2117 |
| 15 | gccctgggcc | acaggcgaga | gtgggcgtgt | cacctgtccc | aggttcccag | caagtctgca | 2177 |
|    | gctgtgcagt | cctggggtcc | ctgaccctgt | cgcccagggg | gcgtgctgtc | cagcaggggc | 2237 |
|    | cctgccttgc | aaggaacgtc | tetteeggeg | gctgggccgc | tcctgcctgg | tctgggctgt | 2297 |
|    | gtgtggcgcc | ctttcctcct | tgtttgttcc | tctgtgttct | gtgtgcgtct | taagcaataa | 2357 |
|    | agcgtggccg | tggctcgcg  |            |            |            |            | 2376 |

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252/346

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<222> (110)..(1102)

5 <400> 114

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geagegeeeg egtagatege tteggeeggg ttetaegeee ggeteaact atg age egg 118
Met Ser Arg

1

tgc gcc cag gcg gcg gaa gtg gcg gcc aca gtg cca ggt gcc ggc gtc 166
Cys Ala Gln Ala Ala Glu Val Ala Ala Thr Val Pro Gly Ala Gly Val

10 15

ggg aac gtg ggg ctg cgg ccc ccc atg gtg ccc cgt cag gcg tcc ttc 214
Gly Asn Val Gly Leu Arg Pro Pro Met Val Pro Arg Gln Ala Ser Phe

15 20 25 30 35

ttc ccg ccg ccg gtg ccg aac ccc ttc gtg cag cag acg cag atc ggc 262
Phe Pro Pro Pro Val Pro Asn Pro Phe Val Gln Gln Thr Gln Ile Gly

40 45 50

tcc gcg agg cgg gtc cag att gtc ctt ctt ggg att atc ttg ctt cca 310

Ser Ala Arg Arg Val Gln Ile Val Leu Leu Gly Ile Ile Leu Leu Pro

55 60 65

att cgt gtc tta ttg gtt gcg tta att tta tta ctt gca tgg cca ttt 358

Ile Arg Val Leu Leu Val Ala Leu Ile Leu Leu Leu Ala Trp Pro Phe

70 75 80

gct gca att tca aca gta tgc tgt cct gaa aag ctg acc cac cca ata 406

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|    | Ala                  | Ala | Ile | Ser | Thr | Val | Cys | Cys | Pro | Glu | Lys | Leu | Thr | His | Pro | Ile |     |
|----|----------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    |                      | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |     |     |     |     |
|    | act                  | ggt | tgg | agg | agg | aaa | att | act | caa | aca | gct | ttg | aaa | ttt | ctg | ggt | 454 |
|    | Thr                  | Gly | Trp | Arg | Arg | Lys | Ile | Thr | Gln | Thr | Ala | Leu | Lys | Phe | Leu | Gly |     |
| 5  | 100                  |     |     |     |     | 105 |     |     |     |     | 110 |     |     |     |     | 115 |     |
|    | cgt                  | gct | atg | ttc | ttt | tca | atg | gga | ttt | ata | gtt | gct | gta | aaa | gga | aag | 502 |
|    | Arg                  | Ala | Met | Phe | Phe | Ser | Met | Gly | Phe | Ile | Val | Ala | Val | Lys | Gly | Lys |     |
|    |                      |     |     |     | 120 |     |     |     |     | 125 |     |     |     |     | 130 |     |     |
|    | att                  | gca | agt | cct | ttg | gaa | gca | cca | gtt | ttt | gtt | gct | gcc | cct | cat | tca | 550 |
| 10 | Ile                  | Ala | Ser | Pro | Leu | Glu | Ala | Pro | Val | Phe | Val | Ala | Ala | Pro | His | Ser |     |
|    |                      |     |     | 135 |     |     |     |     | 140 |     |     |     |     | 145 |     |     |     |
|    | aca                  | ttc | ttt | gat | gga | att | gcc | tgt | gtt | gta | gct | ggg | tta | cct | tct | ata | 598 |
|    | Thr                  | Phe | Phe | Asp | Gly | Ile | Ala | Cys | Val | Val | Ala | Gly | Leu | Pro | Ser | Ile |     |
|    |                      |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |     |     | •   | •   |
| 15 |                      |     |     |     |     |     | gca |     |     |     |     |     |     |     |     |     | 646 |
|    | Val                  |     | Arg | Asn | Glu | Asn | Ala | Gln | Val | Pro | Leu | Ile | Gly | Arg | Leu | Leu |     |
|    |                      | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |     |     |     |     |
|    |                      |     |     |     |     |     | ttg |     |     |     |     |     |     |     |     | _   | 694 |
|    |                      | Ala | Val | Gln | Pro | Val | Leu | Val | Ser | Arg | Val | Asp | Pro | Asp | Ser | Arg |     |
| 20 | 180                  |     |     |     |     | 185 |     |     |     |     | 190 |     |     |     |     | 195 |     |
|    |                      |     |     |     |     |     | ata |     |     |     |     |     |     |     |     |     | 742 |
|    | Lys                  | Asn | Thr | Ile |     | Glu | Ile | Ile | Lys | Arg | Thr | Thr | Ser | Gly | Gly | Glu |     |
|    |                      |     |     |     | 200 |     |     |     |     | 205 |     |     |     |     | 210 |     |     |
| 25 |                      |     |     |     |     |     | ttc |     |     |     |     |     |     |     |     |     | 790 |
| 25 | $\operatorname{Trp}$ | Pro | Gln | Ile | Leu | Val | Phe | Pro | Glu | Glv | Thr | Cvs | Thr | Asn | Arσ | Ser |     |

4

|    |      |      |      | 215  |      |      |     |     | 220  |      |      |      |      | 225   |      |      |      |
|----|------|------|------|------|------|------|-----|-----|------|------|------|------|------|-------|------|------|------|
|    | tgt  | ttg  | att  | act  | ttt  | aaa  | cca | gga | gcc  | ttc  | att  | cca  | gga  | gtt   | cca  | gtg  | 838  |
|    | Cys  | Leu  | Ile  | Thr  | Phe  | Lys  | Pro | Gly | Ala  | Phe  | Ile  | Pro  | Gly  | Val   | Pro  | Val  |      |
|    |      |      | 230  |      |      |      |     | 235 |      |      |      |      | 240  |       |      |      |      |
| 5  | cag  | cca  | gtc  | ctc  | ctc  | aga  | tac | cca | aac  | aag  | ctg  | gat  | act  | gtg   | acc  | tgg  | 886  |
|    | Gln  | Pro  | Val  | Leu  | Leu  | Arg  | Tyr | Pro | Asn  | Lys  | Leu  | Asp  | Thr  | Val   | Thr  | Trp  |      |
|    |      | 245  |      |      |      |      | 250 |     |      |      |      | 255  |      |       |      |      |      |
|    | aca  | tgg  | caa  | gga  | tat  | aca  | ttc | att | cag  | ctt  | tgt  | atg  | ctt  | act   | ttc  | tgc  | 934  |
|    | Thr  | Trp  | Gln  | Gly  | Tyr  | Thr  | Phe | Ile | Gln  | Leu  | Cys  | Met  | Leu  | Thr   | Phe  | Cys  |      |
| 10 | 260  |      |      |      |      | 265  | •   |     |      |      | 270  |      |      |       |      | 275  |      |
|    | cag  | ctc  | ttc  | aca  | aag  | gta  | gaa | gtt | gag  | atg  | ttt  | ctg  | ttc  | ttt   | tgg  | gaa  | 982  |
|    | Gln  | Leu  | Phe  | Thr  | Lys  | Val  | Glu | Val | Glu  | Met  | Phe  | Leu  | Phe  | Phe   | Trp  | Glu  |      |
|    |      |      |      |      | 28.0 |      |     |     |      | 285  |      |      |      |       | 290  |      |      |
|    | gga  | agc  | agc  | aag  | cat  | tgt  | tta | aaa | ata  | tct  | tcc  | ttc  | ttt  | tgc   | att  | ttt  | 1030 |
| L5 | Gly  | Ser  | Ser  | Lys  | His  | Cys  | Leu | Lys | Ile  | Ser  | Ser  | Phe  | Phe  | Cys   | Ile  | Phe  |      |
|    |      |      |      | 295  |      |      |     |     | 300  |      |      |      |      | 305   |      |      |      |
|    | tct  | ctt  | cga  | aga  | ttt  | aaa  | aga | aga | att  | aca  | caa  | aga  | act  | aga   | act  | gca  | 1078 |
|    | Ser  | Leu  | Arg  | Arg  | Phe  | Lys  | Arg | Arg | Ile  | Thr  | Gln  | Arg  | Thr  | Arg   | Thr  | Ala  |      |
|    |      |      | 310  |      |      |      |     | 315 |      |      |      |      | 320  |       |      |      |      |
| 20 | cat  | ttg  | tta  | aga  | ttg  | tcc  | ttt | taa | aatt | attt | tc t | gtta | caag | gg aa | aaaa | taaa | 1132 |
|    | His  | Leu  | Leu  | Arg  | Leu  | Ser  | Phe |     |      |      |      |      |      |       |      |      |      |
|    |      | 325  |      |      |      |      | 330 |     |      |      |      |      |      |       |      |      |      |
|    | agat | tgat | ta t | agto | tcat | a at | :t  |     |      |      |      |      |      |       |      |      | 1155 |

255/346

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Met Ala Leu Pro Pro Gly Pro Ala Ala Leu Arg His Thr

1 5 10

ctg ctg ctc ctg cca gcc ctt ctg agc tca ggt ggg cct ggc acc ccc 157

Leu Leu Leu Pro Ala Leu Leu Ser Ser Gly Gly Pro Gly Thr Pro

15 20 25

aga ttg gcc tgg tat ctg gat gga cag ctg cag gag gcc agc acc tca 205

Arg Leu Ala Trp Tyr Leu Asp Gly Gln Leu Gln Glu Ala Ser Thr Ser

30 35 40 45

20 aga ctg ctg agc gtg gga ggg gag gcc ttc tct gga ggc acc agc acc 253

Arg Leu Leu Ser Val Gly Gly Glu Ala Phe Ser Gly Gly Thr Ser Thr

50 55 60

ttc act gtc act gcc cat cgg gcc cag cat gag ctc aac tgc tct ctg 301
Phe Thr Val Thr Ala His Arg Ala Gln His Glu Leu Asn Cys Ser Leu

25 65 70 75

|    | cag | gac | CCC | aga | agt | ggc | cga | tca | gcc | aac | gcc | tct | gtc | atc | ctt | aat | 349 |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Gln | Asp | Pro | Arg | Ser | Gly | Arg | Ser | Ala | Asn | Ala | Ser | Val | Ile | Leu | Asn |     |
|    |     |     | 80  |     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     |
|    | gtg | caa | ttc | aag | cca | gag | att | gcc | caa | gtc | ggc | gcc | aag | tac | cag | gaa | 397 |
| 5  | Val | Gln | Phe | Lys | Pro | Glu | Ile | Ala | Gln | Val | Gly | Ala | Lys | Tyr | Gln | Glu |     |
|    |     | 95  |     |     |     |     | 100 |     |     |     |     | 105 |     |     |     |     |     |
|    | gct | cag | ggc | cca | ggc | ctc | ctg | gtt | gtc | ctg | ttt | gcc | ctg | gtg | cgt | gcc | 445 |
|    | Ala | Gln | Gly | Pro | Gly | Leu | Leu | Val | Val | Leu | Phe | Ala | Leu | Val | Arg | Ala |     |
|    | 110 |     |     |     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |
| 10 | aac | ccg | ccg | gcc | aat | gtc | acc | tgg | atc | gac | cag | gat | ggg | cca | gtg | act | 493 |
|    | Asn | Pro | Pro | Ala | Asn | Val | Thr | Trp | Ile | Asp | Gln | Asp | Gly | Pro | Val | Thr |     |
|    |     |     |     |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |
|    | gtc | aac | acc | tct | gac | ttc | ctg | gtg | ctg | gat | gcg | cag | aac | tac | ccc | tgg | 543 |
|    | Val | Asn | Thr | Ser | Asp | Phe | Leu | Val | Leu | Asp | Ala | Gln | Asn | Tyr | Pro | Trp |     |
| 15 |     |     |     | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |
|    | ctc | acc | aac | cac | acg | gtg | cag | ctg | cag | ctc | cgc | agc | ctg | gca | cac | aac | 589 |
|    | Leu | Thr | Asn | His | Thr | Val | Gln | Leu | Gln | Leu | Arg | Ser | Leu | Ala | His | Asn |     |
|    |     |     | 160 |     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     |
|    | ctc | tcg | gtg | gtg | gcc | acc | aat | gac | gtg | ggt | gtc | acc | agt | gcg | tcg | ctt | 637 |
| 20 | Leu | Ser | Val | Val | Ala | Thr | Asn | Asp | Val | Gly | Val | Thr | Ser | Ala | Ser | Leu |     |
|    |     | 175 |     |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     |     |
|    | cca | gcc | cca | ggg | ctt | ctg | gct | acc | cgg | gtg | gaa | gtg | cca | ctg | ctg | ggc | 685 |
|    | Pro | Ala | Pro | Gly | Leu | Leu | Ala | Thr | Arg | Val | Glu | Val | Pro | Leu | Leu | Gly |     |
|    | 190 |     |     |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |
| 25 | att | gtt | gtg | gct | gct | ggg | ctt | gca | ctg | ggc | acc | ctc | gtg | ggg | ttc | agc | 733 |

|    | Ile | Val | Val | Ala   | Ala | Gly | Leu | Ala | Leu | Gly | Thr | Leu | Val | Gly | Phe | Ser |      |
|----|-----|-----|-----|-------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|    |     |     |     |       | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |      |
|    | acc | ttg | gtg | gcc   | tgc | ctg | gtc | tgc | aga | aaa | gag | aag | aaa | acc | aaa | ggc | 781  |
|    | Thr | Leu | Val | Ala   | Cys | Leu | Val | Cys | Arg | Lys | Glu | Lys | Lys | Thr | Lys | Gly |      |
| 5  |     |     |     | 225   |     |     |     |     | 230 |     |     |     |     | 235 |     |     |      |
|    | ccc | tcc | cgg | cac   | cca | tct | ctg | ata | tca | agt | gac | tcc | aac | aac | cta | aaa | 829  |
|    | Pro | Ser | Arg | His   | Pro | Ser | Leu | Ile | Ser | Ser | Asp | Ser | Asn | Asn | Leu | Lys |      |
|    |     |     | 240 |       |     |     |     | 245 |     |     |     |     | 250 |     |     |     |      |
|    | ctc | aac | aac | gtg   | cgc | ctg | cca | cgg | gag | aac | atg | tcc | ctc | ccg | tcc | aac | 877  |
| 10 | Leu | Asn | Asn | Val   | Arg | Leu | Pro | Arg | Glu | Asn | Met | Ser | Leu | Pro | Ser | Asn | ,    |
|    |     | 255 |     |       |     |     | 260 |     |     |     |     | 265 |     |     |     |     |      |
|    | ctt | cag | ctc | aat   | gac | ctc | act | cca | gat | tcc | aga | gca | gtg | aaa | cca | gca | 925  |
|    | Leu | Gln | Leu | Asn   | Asp | Leu | Thr | Pro | Asp | Ser | Arg | Ala | Val | Lys | Pro | Ala |      |
|    | 270 |     |     |       |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |      |
| 15 | gac | cgg | cag | atg   | gct | cag | aac | aac | agc | cgg | cca | gag | ctt | ctg | gac | ccg | 973  |
|    | Asp | Arg | Gln | Met   | Ala | Gln | Asn | Asn | Ser | Arg | Pro | Glu | Leu | Leu | Asp | Pro |      |
|    |     |     |     |       | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |      |
|    | gag | ccc | ggc | ggc   | ctc | ctc | acc | agc | caa | gca | tgt | ctc | ctc | cac | cac | ggg | 1021 |
|    | Glu | Pro | Gly | Gly   | Leu | Leu | Thr | Ser | Gln | Ala | Cys | Leu | Leu | His | His | Gly |      |
| 20 |     |     |     | 305   |     |     |     |     | 310 |     |     |     |     | 315 |     |     |      |
|    | acc | cca | gcc | ctg   | acc | aac | cca | tgg | ttg | cct | cat | cag | cag | gaa | ggt | gcc | 1069 |
|    | Thr | Pro | Ala | Leu   | Thr | Asn | Pro | Trp | Leu | Pro | His | Gln | Gln | Glu | Gly | Ala |      |
|    |     |     | 320 |       |     |     |     | 325 |     |     |     |     | 330 |     |     |     |      |
|    | ctt | cct | gga | . gga | tgg | tcg | cca | cag | gca | cat | aat | tca | aca | gtg | tgg | aag | 1117 |
| 25 | Leu | Pro | Gly | Gly   | Trp | Ser | Pro | Gln | Ala | His | Asn | Ser | Thr | val | Trp | Lys |      |

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335 340 345

ctt tag gggaacatgg agaaagaagg agaccacata ccccaaagtg acctaagaac 1173

350

actttaaaaa gcaacatgta aatgattgga aattaatata gtacagaata tattttccc 1233
ttgttgagat cttcttttgt aatgtttttc atgttactgc ctagggcggt gctgagcaca 1293
cagcaagttt aataaacttg actgaattca tttaat 1329

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<400> 116

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actcactggt gtcatcaggc ccctcc atg aat gag aca aac aaa aca ctt gtt 173
Met Asn Glu Thr Asn Lys Thr Leu Val

5

ggg cct tcg gag ctc ccc aca gcg tct gct gtg gcc cct ggc cca ggc 221

25 Gly Pro Ser Glu Leu Pro Thr Ala Ser Ala Val Ala Pro Gly Pro Gly

|    | 10  |       |      |      |       | 15    |       |       |       |       | 20    |       |       |              |      | 25      |       |
|----|-----|-------|------|------|-------|-------|-------|-------|-------|-------|-------|-------|-------|--------------|------|---------|-------|
|    | act | ggg   | gct  | cgg  | gca   | tgg   | cct   | gtg   | ctg   | gta   | gga   | ttt   | gtg   | ctg          | ggg  | gct     | 269   |
|    | Thr | Gly   | Ala  | Arg  | Ala   | Trp   | Pro   | Val   | Leu   | Val   | Gly   | Phe   | Val   | Leu          | Gly  | Ala     |       |
|    |     |       |      |      | 30    |       |       |       |       | 35    |       |       |       |              | 40   |         |       |
| 5  | gtg | gtc   | ctc  | tcg  | ctc   | ctc   | att   | gca   | ctt   | gct   | gcc   | aaa   | tgc   | cac          | ctc  | tgc     | 317   |
|    | Val | Val   | Leu  | Ser  | Leu   | Leu   | Ile   | Ala   | Leu   | Ala   | Ala   | Lys   | Cys   | His          | Leu  | Cys     |       |
|    |     |       |      | 45   |       |       |       |       | 50    |       |       |       |       | 55           |      |         |       |
|    | cgc | cga   | tac  | cat  | gcc   | agc   | tac   | cgg   | cac   | cgc   | cca   | ctg   | cct   | gag          | aca  | gga     | 365   |
|    | Arg | Arg   | Tyr  | His  | Ala   | Ser   | Tyr   | Arg   | His   | Arg   | Pro   | Leu   | Pro   | Glu          | Thr  | Gly     |       |
| 10 |     |       | 60   |      |       |       |       | 65    |       |       |       |       | 70    |              |      |         | •     |
|    | agg | gga   | ggc  | cgc  | cca   | cag   | gtg   | gct   | gaa   | gat   | gag   | gat   | gat   | gat          | ggc  | ttc     | 413   |
|    | Arg | Gly   | Gly  | Arg  | Pro   | Gln   | Val   | Ala   | Glu   | Asp   | Glu   | Asp   | Asp   | Asp          | Gly  | Phe     |       |
|    |     | 75    |      |      |       |       | 80    |       |       |       |       | 85    |       |              |      |         |       |
|    | atc | gag   | gac  | aat  | tac   | att   | cag   | cct   | ggg   | act   | ggc   | gag   | ctg   | ggg          | aca  | gag     | 461   |
| 15 | Ile | Glu   | Asp  | Asn  | Tyr   | Ile   | Gln   | Pro   | Gly   | Thr   | Gly   | Glu   | Leu   | Gly          | Thr  | Glu     |       |
|    | 90  |       |      |      |       | 95    |       |       |       |       | 100   |       |       |              |      | 105     |       |
|    | ggt | ago   | agg  | gac  | cac   | ttc   | tcc   | ctc   | tga   | gct   | .ccca | tct   | ttag  | acco         | tc   |         | 508   |
|    | Gly | Ser   | Arg  | Asp  | His   | Phe   | Ser   | Leu   |       |       |       |       |       |              |      |         |       |
|    |     |       |      |      | 110   | )     |       |       |       |       |       |       |       |              |      |         |       |
| 20 | ccc | acto  | cct  | ccat | .gcct | ga c  | agct  | taag  | g ac  | agtg  | gtta  | tga   | cato  | <b>199</b> 9 | gcct | tgaacc  | : 568 |
|    | tca | ıggga | cag  | aggt | .ggct | gg g  | gctt  | aaag  | g tt  | .ggcc | aggg  | ato   | gagt  | caaa         | ccc  | acttcc  | 628   |
|    | cto | jacac | tag  | ccaç | caaa  | agt g | jacaa | tgac  | c ct  | ctct  | tgct  | caa   | ataad | ctct         | caad | tgttcc  | 688   |
|    | cto | gctgt | tct  | cago | gataa | aag d | caaa  | ıcaaa | ıg go | ttga  | agtgt | gga   | acata | aagg         | ccct | ctgtga  | 748   |
|    | tca | atgco | ctct | cggd | ctcl  | tg q  | tttc  | tttt  | c ti  | gcct  | tcc   | c cta | actti | tact         | gtc  | gaaatca | a 808 |
| 25 | ato | rctat | tct  | ccct | ccc   | acc a | actto | ccat  | g ca  | agtti | ccc   | age   | gcac  | cttt         | gct  | cacatto | 868   |

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gtcccctgc ctacgctact cttcccctaa atcctctatg actgtgatgg cctgcctacc 928
tgccagcatt tcaaatatgc ccagatggta acatttgtgc aggtgaaaac cagtgccaag 988
cttccttttt ttttttttt cctgagacgg agtctcactc tgttgcccag gctggagtgc 1048
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ttttagtaga gacgaggttt cgccatattg gccaggatgg tctcgaactc ttgacctcag 1228
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Met Ala Leu Leu Ser Arg Pro Ala Leu Thr Leu Leu Leu

25

1

5

10

|    | ctc | atg | gcc | gct | gtt | gtc | agg | tgc | cag | gag | cag | gcc | cag | acc | acc | gac | 219 |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Leu | Met | Ala | Ala | Val | Val | Arg | Cys | Gln | Glu | Gln | Ala | Gln | Thr | Thr | Asp |     |
|    | 15  |     |     |     |     | 20  |     |     |     |     | 25  |     | ,   |     |     | 30  |     |
|    | tgg | aga | gcc | acc | ctg | aag | acc | atc | cgg | aac | ggc | gtt | cat | aag | ata | gac | 267 |
| 5  | Trp | Arg | Ala | Thr | Leu | Lys | Thr | Ile | Arg | Asn | Gly | Val | His | Lys | Ile | Asp |     |
|    |     |     |     |     | 35  |     |     |     |     | 40  | ٠   |     |     |     | 45  |     |     |
|    | acg | tac | ctg | aac | gcc | gcc | ttg | gac | ctc | ctg | gga | ggc | gag | gac | ggt | ctc | 315 |
|    | Thr | Tyr | Leu | Asn | Ala | Ala | Leu | Asp | Leu | Leu | Gly | Gly | Glu | Asp | Gly | Leu |     |
|    |     |     |     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |
| 10 | tgc | cag | tat | aaa | tgc | agt | gac | gga | tct | aag | cct | ttc | cca | cgt | tat | ggt | 363 |
|    | Cys | Gln | Tyr | Lys | Cys | Ser | Asp | Gly | Ser | Lys | Pro | Phe | Pro | Arg | Tyr | Gly |     |
|    |     |     | 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     |
|    | tat | aaa | ccc | tcc | cca | ccg | aat | gga | tgt | ggc | tct | cca | ctg | ttt | ggt | gtt | 411 |
|    | Tyr | Lys | Pro | Ser | Pro | Pro | Asn | Gly | Cys | Gly | Ser | Pro | Leu | Phe | Gly | Val |     |
| 15 |     | 80  |     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     |     |
|    | cat | ctt | aac | att | ggt | atc | cct | tcc | ctg | aca | aag | tgt | tgc | aac | caa | cac | 459 |
|    | His | Leu | Asn | Ile | Gly | Ile | Pro | Ser | Leu | Thr | Lys | Cys | Cys | Asn | Gln | His |     |
|    | 95  |     |     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |
|    | gac | agg | tgc | tat | gaa | acc | tgt | ggc | aaa | agc | aag | aat | gac | tgt | gat | gaa | 507 |
| 20 | Asp | Arg | Cys | Tyr | Glu | Thr | Cys | Gly | Lys | Ser | Lys | Asn | Asp | Сув | Asp | Glu |     |
|    |     |     |     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |
|    | gaa | ttc | cag | tat | tgc | ctc | tcc | aag | atc | tgc | cga | gat | gta | cag | aaa | aca | 555 |
|    | Glu | Phe | Gln | Tyr | Cys | Leu | Ser | Lys | Ile | Cys | Arg | Asp | Val | Gln | Lys | Thr |     |
|    |     |     |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |
| 25 | cta | gga | cta | act | cag | cat | gtt | cag | gca | tgt | gaa | aca | aca | gtg | gag | ctc | 603 |

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|    | Leu  | Gly   | Leu   | Thr   | Gln   | His   | Val   | Gln   | Ala   | Суѕ   | Glu  | Thr  | Thr   | Val   | Glu   | Leu    |      |
|----|------|-------|-------|-------|-------|-------|-------|-------|-------|-------|------|------|-------|-------|-------|--------|------|
|    |      |       | 145   |       |       |       |       | 150   |       |       |      |      | 155   |       |       |        |      |
|    | ttg  | ttt   | gac   | agt   | gtt   | ata   | cat   | tta   | ggt   | tgt   | aaa  | cca  | tat   | ctg   | gac   | agc    | 651  |
|    | Leu  | Phe   | Asp   | Ser   | Val   | Ile   | His   | Leu   | Gly   | Cys   | Lys  | Pro  | Tyr   | Leu   | Asp   | Ser    |      |
| 5  |      | 160   |       |       |       |       | 165   |       |       |       |      | 170  |       |       |       |        |      |
|    | caa  | cga   | gcc   | gca   | tgc   | agg   | tgt   | cat   | tat   | gaa   | gaa  | aaa  | act   | gat   | ctt   | taa    | 699  |
|    | Gln  | Arg   | Ala   | Ala   | Cys   | Arg   | Cys   | His   | Tyr   | Glu   | Glu  | Lys  | Thr   | Asp   | Leu   |        |      |
|    | 175  |       |       |       |       | 180   |       |       |       |       | 185  |      |       |       |       | 190    |      |
|    | agga | agato | jec d | jaca  | gctag | gt ga | acaga | atgaa | a gat | ggaa  | agaa | cata | acct  | ttt   | gacaa | aataac | 759  |
| 10 | taat | gttt  | tt a  | caa   | cataa | aa ad | ctgto | cttat | : ttt | tgto  | gaaa | ggat | tati  | ttt   | gagad | ccttaa | 819  |
|    | aata | attt  | at a  | tctt  | gato  | yt ta | aaaa  | cctca | aag   | rcaaa | aaa  | agto | gaggg | gag . | atagi | gaggg  | 879  |
|    | gago | gcac  | cgc t | tgto  | cttct | c ag  | gtat  | ctto  | ccc   | agca  | attg | ctc  | ctta  | act   | tagta | atgcca | 939  |
|    | aato | tctt  | ga d  | caat  | catca | aa aa | acaa  | agtgo | tt:   | ıttta | agcg | gaga | attt  | ttg : | aaaa  | gaggaa | 999  |
|    | tata | ataac | etc a | attt  | tcac  | a ad  | caca  | attta | a cca | aaaa  | aag  | agat | caaa  | ata · | taaaa | attcat | 1059 |
| 15 | cata | atgt  | ct g  | jttca | acat  | t at  | ctta  | atttg | g gaa | aato  | iggg | aaat | tato  | cac f | ttaca | agtat  | 1119 |
|    | ttgt | ttac  | cta t | gaaa  | atttt | a aa  | ataca | catt  | : tat | gcct  | ag   |      |       |       |       |        | 1158 |
|    |      |       |       |       | •     |       |       |       |       |       |      |      |       |       |       |        |      |
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<213> Homo sapiens

<220>

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25 <222> (26)..(859)

PCT/JP00/09359 WO 01/49728

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Met Ser Pro Leu Leu Gly Leu Arg Ser

gag ctg cag gac acc tgc acc tcg ctg gga ctg atg ctg tcg gtg gtg Glu Leu Gln Asp Thr Cys Thr Ser Leu Gly Leu Met Leu Ser Val Val 

ctg ctc atg ggg ctg gcc cgc gta gtc gcc cgg cag cag ctg cac agg Leu Leu Met Gly Leu Ala Arg Val Val Ala Arg Gln Gln Leu His Arg

ccq qtq gcc cac gcc ttc gtc ctg gag ttt cta gcc acc ttc cag ctc Pro Val Ala His Ala Phe Val Leu Glu Phe Leu Ala Thr Phe Gln Leu

tgc tgc tgc acc cac gag ctg caa ctg ctg agc gaa cag cac ccc gcg Cys Cys Cys Thr His Glu Leu Gln Leu Ser Glu Gln His Pro Ala

cac ccc acc tgg acg ctg acg ctc gtc tac ttc ttc tcg ctt gtg cat His Pro Thr Trp Thr Leu Thr Leu Val Tyr Phe Phe Ser Leu Val His

> ggc ctg act ctg gtg ggc acg tcc agc aac ccg tgc ggc gtg atg atg Gly Leu Thr Leu Val Gly Thr Ser Ser Asn Pro Cys Gly Val Met Met

> cag atg atg ctg ggg ggc atg tcc ccc gag acg ggt gcg gtg agg cta Gln Met Met Leu Gly Gly Met Ser Pro Glu Thr Gly Ala Val Arg Leu

|    |     |     |     |     | 110 |     |     |     |     | 115 |     |     |     |     | 120 |     |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | ttg | gct | cag | ctg | gtt | agt | gcc | ctg | tgc | agc | agg | tac | tgc | aca | agc | gcc | 436 |
|    | Leu | Ala | Gln | Leu | Val | Ser | Ala | Leu | Cys | Ser | Arg | Tyr | Cys | Thr | Ser | Ala |     |
|    |     |     |     | 125 |     |     |     |     | 130 |     |     |     |     | 135 |     |     |     |
| 5  | ttg | tgg | agc | ttg | ggt | ctg | acc | cag | tat | cac | gtc | agc | gag | agg | agc | ttc | 484 |
|    | Leu | Trp | Ser | Leu | Gly | Leu | Thr | Gln | Tyr | His | Val | Ser | Glu | Arg | Ser | Phe |     |
|    |     |     | 140 |     |     |     |     | 145 |     |     |     |     | 150 |     |     |     |     |
|    | gct | tgc | aag | aat | ccc | atc | cga | gtc | gac | ttg | ctc | aaa | gcg | gtc | atc | aca | 532 |
|    | Ala | Cys | Lys | Asn | Pro | Ile | Arg | Val | Asp | Leu | Leu | Lys | Ala | Val | Ile | Thr |     |
| 10 |     | 155 |     |     |     |     | 160 |     |     |     |     | 165 | Ē   |     |     |     |     |
|    | gag | gcc | gtc | tgc | tcc | ttt | ctc | ttc | cac | agc | gct | ctg | ctg | cac | ttc | cag | 580 |
|    | Glu | Ala | Val | Cys | Ser | Phe | Leu | Phe | His | Ser | Ala | Leu | Leu | His | Phe | Gln |     |
|    | 170 |     |     |     |     | 175 |     |     |     |     | 180 |     |     |     |     | 185 |     |
|    | gaa | gtc | cga | acc | aag | ctt | cgt | atc | cac | ctg | ctg | gct | gca | ctc | atc | acc | 628 |
| 15 | Glu | Val | Arg | Thr | Lys | Leu | Arg | Ile | His | Leu | Leu | Ala | Ala | Leu | Ile | Thr |     |
|    |     |     |     |     | 190 |     |     |     |     | 195 |     |     |     |     | 200 |     |     |
|    | ttt | ttg | gtc | tat | gca | gga | gga | agt | cta | aca | gga | gct | gta | ttt | aat | cca | 676 |
|    | Phe | Leu | Val | Tyr | Ala | Gly | Gly | Ser | Leu | Thr | Gly | Ala | Val | Phe | Asn | Pro |     |
|    |     |     |     | 205 |     |     |     |     | 210 |     |     |     |     | 215 |     |     |     |
| 20 | gct | ttg | gca | ctt | tcg | cta | cat | ttc | atg | tgt | ttt | gat | gaa | gca | ttc | cct | 724 |
|    | Ala | Leu | Ala | Leu | Ser | Leu | His | Phe | Met | Cys | Phe | Asp | Glu | Ala | Phe | Pro |     |
|    |     |     | 220 |     |     |     |     | 225 |     |     |     |     | 230 |     |     |     |     |
|    | cag | ttt | ttt | ata | gta | tac | tgg | ctg | gct | cct | tct | tta | ggt | ata | ttg | ttg | 772 |
|    | Gln | Phe | Phe | Ile | Val | Tyr | Trp | Leu | Ala | Pro | Ser | Leu | Gly | Ile | Leu | Leu |     |
| 25 |     | 235 |     |     |     |     | 240 |     |     |     |     | 245 |     |     |     |     |     |

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atg att ttg atg ttc agc ttt ttc cat ggc tgc ata aca acc ata caa 820

Met Ile Leu Met Phe Ser Phe Phe His Gly Cys Ile Thr Thr Ile Gln

250 255 260 265

tta ata aaa agg aat aac tgt tcc aaa gac tca gac taa catacaggac 869
Leu Ile Lys Arg Asn Asn Cys Ser Lys Asp Ser Asp

270 275

agtccagctg gatgtgataa agattttatc acctcatatg gaaaacaccg gctgcactgg 929
attcatcagt gttaacttcc tttgaggaag ctgccttata gttttcatca ctgggacttt 989
aaaaaaaaat tactgtgaaa atgaggtatt ctgtacttct cagttaagac ttgttctttg 1049
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<211> 1907

<212> DNA

15 <213> Homo sapiens

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<222> (159)..(983)

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<400> 119

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25

Met Gly Lys Ser Leu Ser

|    |     |          |     |     |     |     |     |     |     |     |     | 1   |     |     |     | 5   |     |
|----|-----|----------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | cat | ttg      | cct | ttg | cat | tca | agc | aaa | gaa | gat | gct | tat | gat | gga | gtc | aca | 224 |
|    | Hiș | Leu      | Pro | Leu | His | Ser | Ser | Lys | Glu | Asp | Ala | Tyr | Asp | Gly | Val | Thr |     |
|    |     |          |     | 10  |     |     |     |     | 15  |     |     |     |     | 20  |     |     |     |
| 5  | tct | gaa      | aac | atg | agg | aat | gga | ctg | gtt | aat | agt | gaa | gtc | cat | aat | gaa | 272 |
|    | Ser | Glu      | Asn | Met | Arg | Asn | Gly | Leu | Val | Asn | Ser | Glu | Val | His | Asn | Glu |     |
|    |     |          | 25  |     |     |     |     | 30  |     |     |     |     | 35  |     |     |     |     |
|    | gat | gga      | aga | aat | gga | gat | gtc | tct | cag | ttt | cca | tat | gtg | gaa | ttt | aca | 320 |
|    | Asp | Gly      | Arg | Asn | Gly | Asp | Val | Ser | Gln | Phe | Pro | Tyr | Val | Glu | Phe | Thr |     |
| 10 |     | 40       |     |     |     |     | 45  |     |     |     |     | 50  |     |     |     |     |     |
|    | gga | aga<br>· | gat | agt | gtc | acc | tgc | cct | act | tgt | cag | gga | aca | gga | aga | att | 368 |
|    | Gly | Arg      | Asp | Ser | Val | Thr | Cys | Pro | Thr | Cys | Gln | Gly | Thr | Gly | Arg | Ile |     |
|    | 55  |          |     |     |     | 60  |     |     |     |     | 65  |     |     |     |     | 70  |     |
|    | cct | agg      | ggg | caa | gaa | aac | caa | ctg | gtg | gca | ttg | att | cca | tat | agt | gat | 416 |
| 15 | Pro | Arg      | Gly | Gln | Glu | Asn | Gln | Leu | Val | Ala | Leu | Ile | Pro | Tyr | Ser | Asp |     |
|    |     |          |     |     | 75  |     |     |     |     | 80  |     |     |     |     | 85  |     |     |
|    | cag | aga      | tta | agg | cca | aga | aga | aca | aag | ctg | tat | gtg | atg | gct | tct | gtg | 464 |
|    | Gln | Arg      | Leu | Arg | Pro | Arg | Arg | Thr | Lys | Leu | Tyr | Val | Met | Ala | Ser | Val |     |
|    |     |          |     | 90  |     |     |     |     | 95  |     |     |     |     | 100 |     |     |     |
| 20 | ttt | gtc      | tgt | cta | ctc | ctt | tct | gga | ttg | gct | gtg | ttt | ttc | ctt | ttc | cct | 512 |
|    | Phe | Val      | Cys | Leu | Leu | Leu | Ser | Gly | Leu | Ala | Val | Phe | Phe | Leu | Phe | Pro |     |
|    |     |          | 105 |     |     |     |     | 110 |     |     |     |     | 115 |     |     |     |     |
|    | cgc | tct      | atc | gac | gtg | aaa | tac | att | ggt | gta | aaa | tca | gcc | tat | gtc | agt | 560 |
|    | Arg | Ser      | Ile | Asp | Val | Lys | Tyr | Ile | Gly | Val | Lys | Ser | Ala | Tyr | Val | Ser |     |
| 25 |     | 120      |     |     |     |     | 125 |     |     |     |     | 130 |     |     |     |     |     |

|    | tat | gat   | gtt | cag | aag | cgt    | aca | att | tat | tta   | aat | atc | aca | aac | aca  | cta | 608 |
|----|-----|-------|-----|-----|-----|--------|-----|-----|-----|-------|-----|-----|-----|-----|------|-----|-----|
|    | Tyr | Asp   | Val | Gln | Lys | Arg    | Thr | Ile | Tyr | Leu   | Asn | Ile | Thr | Asn | Thr  | Leu |     |
|    | 135 |       |     |     |     | 140    |     |     |     |       | 145 |     |     |     |      | 150 |     |
|    | aat | ata   | aca | aac | aat | aac    | tat | tac | tct | gtc   | gaa | gtt | gaa | aac | atc  | act | 656 |
| 5  | Asn | Ile   | Thr | Asn | Asn | Asn    | Tyr | Tyr | Ser | Val   | Glu | Val | Glu | Asn | Ile  | Thr |     |
|    |     |       |     |     | 155 |        |     |     |     | 160   |     |     |     |     | 165  |     |     |
|    | gcc | caa   | gtt | caa | ttt | tca    | aaa | aca | gtt | att   | gga | aag | gca | cgc | tta  | aac | 704 |
|    | Ala | Gln   | Val | Gln | Phe | Ser    | Lys | Thr | Val | Ile   | Gly | Lys | Ala | Arg | Leu  | Asn |     |
|    |     |       |     | 170 |     |        |     |     | 175 |       |     |     |     | 180 |      |     |     |
| 10 | aac | ata   | acc | att | att | ggt    | cca | ctt | gat | atg   | aaa | caa | att | gat | tac  | aca | 752 |
|    | Asn | Ile   | Thr | Ile | Ile | Gly    | Pro | Leu | Asp | Met   | Lys | Gln | Ile | Asp | Tyr  | Thr |     |
|    |     |       | 185 |     |     |        |     | 190 |     |       |     |     | 195 |     |      |     |     |
|    | gta | cct   | acc | gtt | ata | gca    | gag | gaa | atg | agt   | tat | atg | tat | gat | ttc  | tgt | 800 |
|    | Val | Pro   | Thr | Val | Ile | Ala    | Glu | Glu | Met | Ser   | Tyr | Met | Tyr | Asp | Phe  | Cys |     |
| 15 |     | 200   |     |     |     |        | 205 |     |     |       |     | 210 |     |     |      |     |     |
|    | act | ctg   | ata | tcc | atc | aaa    | gtg | cat | aac | ata   | gta | ctc | atg | atg | caa  | gtt | 848 |
|    | Thr | Leu   | Ile | Ser | Ile | Lys    | Val | His | Asn | Ile   | Val | Leu | Met | Met | Gln  | Val |     |
|    | 215 | ,     |     |     |     | 220    |     |     |     |       | 225 |     |     |     |      | 230 |     |
|    | act | gtg   | aca | aca | aca | tac    | ttt | ggc | cac | tct   | gaa | cag | ata | tcc | cag  | gag | 896 |
| 20 | Thr | : Val | Thr | Thr | Thr | Tyr    | Phe | Gly | His | Ser   | Glu | Gln | Ile | Ser | Gln  | Glu |     |
|    |     |       |     |     | 235 | ,      |     |     |     | 240   |     |     |     |     | 245  |     |     |
|    | agg | tat   | cag | tat | gto | gac    | tgt | gga | aga | aac   | aca | act | tat | cag | ttg  | ggg | 944 |
|    | Arg | Tyr   | Gln | Tyr | Val | . Asp  | Cys | Gly | Arg | Asn   | Thr | Thr | Tyr | Glr | Leu  | Gly |     |
|    |     |       |     | 250 |     |        |     |     | 255 | ,     |     |     |     | 260 | )    |     |     |
| 25 | cag | , tct | gaa | tat | tta | a 'aat | gta | ctt | cag | r cca | caa | cag | taa | aaa | ctgg | aag | 993 |

#### 268/346

Gln Ser Glu Tyr Leu Asn Val Leu Gln Pro Gln Gln

265 270 275

agatggattt aaagaagaaa tatctattga tatttcctat actctcaatg aagaggtatt 1053 tcctaatagg agaccttaaa ttgaacaaac ctaaagttta cacttctaag agtacagtta 1113 aaagtatgtg gacctgcagt tcttgtaact ctccactctg tgttaatgat atatttgtac 1173 taggatettt taettgaate taaatttaet ggttgattte etteteeage etateeeeta 1233 cagggaaaag ctgatacttc ccctatagta caataaataa ttatttaaaa qtcataqctc 1293 cagtcactac tgaaaacata attttggtga taaaataatt tgagaaactt aatttctgaa 1353 tgtttttata gaaaattact gaaagtctat tactcatgga agacttttaa agaataacct 1413 tttttcctgt tttataaatt cccattgtta tatggtagta tttcagctac acaatatttt 1473 agcttttagc tagacattta tagcttttca tttgttgaaa tggtaatcat ctgcatgttt 1533 ttgtcactta tttcaggtta gtgattgcct aacacttata agccaaaata atctttgcaa 1593 aattccatac ctaaaatttt gaaagcccct aatgttttca cacatctttc tgtattagtt 1653 atagtittgt gaaatctttg tgtgatcttc aaacattatc atttaatgta caatactgta 1713 aataaactgt gcatggcttt tatacagctt tagtaaatgt caaataaagt ggtacagact 1773 cattacaaca agtttctcat aaaaaatacaa taaataggaa aatgaaattc agaaacccat 1833 agactgggaa taggttccag ttacagcttg gatctggcat aaaataaatt tgaaataaaa 1893 tattttgatg ctcc 1907

20 <210> 120

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10

15

<211> 1816

<212> DNA

<213> Homo sapiens

25 <220>

#### 269/346

<221> CDS

<222> (134)..(1306)

15

80

<400> 120

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10 Leu Arg Phe Leu Phe Leu Gly Leu Ser Ala Leu Ala Pro Pro Ser Arg

> 20 25

gcc cag ctg caa ctg cac ttg ccc gcc aac cgg ttg cag gcg gtg gag 265 Ala Gln Leu Gln Leu His Leu Pro Ala Asn Arg Leu Gln Ala Val Glu

15 30 35 40

> gga ggg gaa gtg gtg ctt cca gcg tgg tac acc ttg cac ggg gag gtg 313 Gly Gly Glu Val Val Leu Pro Ala Trp Tyr Thr Leu His Gly Glu Val

45 50 55 60

tct tca tcc cag cca tgg gag gtg ccc ttt gtg atg tgg ttc ttc aaa 361 20 Ser Ser Ser Gln Pro Trp Glu Val Pro Phe Val Met Trp Phe Phe Lys

> 65 70 75

cag aaa gaa aag gag gat cag gtg ttg tcc tac atc aat ggg gtc aca 409 Gln Lys Glu Lys Glu Asp Gln Val Leu Ser Tyr Ile Asn Gly Val Thr

90

85

25 aca age aaa cet gga gta tee ttg gte tae tee atg eec tee egg aac

|    | Thr | Ser | Lys | Pro | Gly | Val | Ser | Leu | Val | Tyr | Ser | Met | Pro | Ser | Arg | Asn |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    |     |     | 95  |     |     |     |     | 100 |     |     |     |     | 105 |     |     |     |     |
|    | ctg | tcc | ctg | cgg | ctg | gag | ggt | ctc | cag | gag | aaa | gac | tcţ | ggc | ccc | tac | 505 |
|    | Leu | Ser | Leu | Arg | Leu | Glu | Gly | Leu | Gln | Glu | Lys | Asp | Ser | Gly | Pro | Tyr |     |
| 5  |     | 110 |     |     |     |     | 115 |     |     |     |     | 120 |     |     |     |     |     |
|    | agc | tgc | tcc | gtg | aat | gtg | caa | gac | aaa | caa | ggc | aaa | tct | agg | ggc | cac | 553 |
|    | Ser | Cys | Ser | Val | Asn | Val | Gln | Asp | Lys | Gln | Gly | Lys | Ser | Arg | Gly | His |     |
|    | 125 |     |     |     |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |
|    | agc | atc | aaa | acc | tta | gaa | ctc | aat | gta | ctg | gtt | cct | cca | gct | cct | cca | 601 |
| 10 | Ser | Ile | Lys | Thr | Leu | Glu | Leu | Asn | Val | Leu | Val | Pro | Pro | Ala | Pro | Pro |     |
|    |     |     |     |     | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |
|    | tcc | tgc | cgt | ctc | cag | ggt | gtg | ccc | cat | gtg | ggg | gca | aac | gtg | acc | ctg | 649 |
|    | Ser | Cys | Arg | Leu | Gln | Gly | Val | Pro | His | Val | Gly | Ala | Asn | Val | Thr | Leu |     |
|    |     |     |     | 160 |     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |
| 15 | agc | tgc | cag | tct | cca | agg | agt | aag | ccc | gct | gtc | caa | tac | cag | tgg | gat | 697 |
|    | Ser | Cys | Gln | Ser | Pro | Arg | Ser | Lys | Pro | Ala | Val | Gln | Tyr | Gln | Trp | Asp |     |
|    |     |     | 175 |     |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     |
|    | cgg | cag | ctt | cca | tcc | ttc | cag | act | ttc | ttt | gca | cca | gca | tta | gat | gtc | 745 |
|    | Arg | Gln | Leu | Pro | Ser | Phe | Gln | Thr | Phe | Phe | Ala | Pro | Ala | Leu | Asp | Val |     |
| 20 |     | 190 |     |     |     |     | 195 |     |     |     |     | 200 |     |     |     |     |     |
|    | atc | cgt | ggg | tct | tta | agc | ctc | acc | aac | ctt | tcg | tct | tcc | atg | gct | gga | 793 |
|    | Ile | Arg | Gly | Ser | Leu | Ser | Leu | Thr | Asn | Leu | Ser | Ser | Ser | Met | Ala | Gly |     |
|    | 205 |     |     |     |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |
|    | gtc | tat | gtc | tgc | aag | gcc | cac | aat | gag | gtg | ggc | act | gcc | caa | tgt | aat | 841 |
| 25 | Val | Tyr | Val | Cys | Lys | Ala | His | Asn | Glu | Val | Gly | Thr | Ala | Gln | Cys | Asn | •   |

|    |     |     |     |     | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |      |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|    | gtg | acg | ctg | gaa | gtg | agc | aca | ggg | cct | gga | gct | gca | gtg | gtt | gct | gga | 889  |
|    | Val | Thr | Leu | Glu | Val | Ser | Thr | Gly | Pro | Gly | Ala | Ala | Val | Val | Ala | Gly |      |
|    |     |     |     | 240 |     |     |     |     | 245 |     |     |     |     | 250 |     |     |      |
| 5  | gct | gtt | gtg | ggt | acc | ctg | gtt | gga | ctg | ggg | ttg | ctg | gct | ggg | ctg | gtc | 937  |
|    | Ala | Val | Val | Gly | Thr | Leu | Val | Gly | Leu | Gly | Leu | Leu | Ala | Gly | Leu | Val |      |
|    |     | •   | 255 |     |     |     |     | 260 |     |     |     |     | 265 |     |     |     |      |
|    | ctc | ttg | tac | cac | tgc | cgg | ggc | aag | gcc | ctg | gag | gag | cca | gcc | aat | gat | 985  |
|    | Leu | Leu | Tyr | His | Cys | Arg | Gly | Lys | Ala | Leu | Glu | Glu | Pro | Ala | Asn | Asp |      |
| 10 |     | 270 |     |     |     |     | 275 |     |     |     |     | 280 |     |     |     |     |      |
|    | atc | aag | gag | gat | gcc | att | gct | ccc | cgg | acc | ctg | ccc | tgg | ccc | aag | agc | 1033 |
|    | Ile | Lys | Glu | Asp | Ala | Ile | Ala | Pro | Arg | Thr | Leu | Pro | Trp | Pro | Lys | Ser |      |
|    | 285 |     |     |     |     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |      |
|    | tca | gac | aca | atc | tcc | aag | aat | ggg | acc | ctt | tcc | tct | gtc | acc | tcc | gca | 1081 |
| 15 | Ser | Asp | Thr | Ile | Ser | Lys | Asn | Gly | Thr | Leu | Ser | Ser | Val | Thr | Ser | Ala |      |
|    |     |     |     |     | 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |      |
|    | cga | gcc | ctc | cgg | cca | ccc | cat | ggc | cct | ccc | agg | cct | ggt | gca | ttg | acc | 1129 |
|    | Arg | Ala | Leu | Arg | Pro | Pro | His | Gly | Pro | Pro | Arg | Pro | Gly | Ala | Leu | Thr |      |
|    |     |     |     | 320 |     |     |     |     | 325 |     |     |     |     | 330 |     |     |      |
| 20 | ccc | acg | ccc | agt | ctc | tcc | agc | cag | gcc | ctg | ccc | tca | cca | aga | ctg | ccc | 1177 |
|    | Pro | Thr | Pro | Ser | Leu | Ser | Ser | Gln | Ala | Leu | Pro | Ser | Pro | Arg | Leu | Pro |      |
|    |     |     | 335 |     |     |     |     | 340 |     |     |     |     | 345 |     |     |     |      |
|    | acg | aca | gat | ggg | gcc | cac | cct | caa | cca | ata | tcc | ccc | atc | cct | ggt | ggg | 1225 |
|    | Thr | Thr | Asp | Gly | Ala | His | Pro | Gln | Pro | Ile | Ser | Pro | Ile | Pro | Gly | Gly |      |
| 25 |     | 350 |     |     |     |     | 355 |     |     |     |     | 360 |     |     |     |     |      |

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gtt tct tcc tct ggc ttg agc cgc atg ggt gct gtg cct gtg atg gtg 1273

Val Ser Ser Ser Gly Leu Ser Arg Met Gly Ala Val Pro Val Met Val

365 370 375 380

cct gcc cag agt caa gct ggc tct ctg gta tga tgaccccacc actcattggc 1326

Pro Ala Gln Ser Gln Ala Gly Ser Leu Val

385 390

taaaagattt ggggtetete etteetatag gggteacete tageacagag geetgagtea 1386
tgggaaagag teacacteet gaceettagt actetgeece cacetetett tactgtggga 1446
aaaceatete agtaagacet aagtgteeag gagacagaag gagaagagga agtggatetg 1506
gaattgggag gageeteeae eeaceeetga eteeteetta tgaageeage tgetgaaatt 1566
agetacteae caagagtgag gggeagagae tteeagteae tgagteteee aggeeeett 1626
gatetgtace eeaceeetat etaacaceae eettggetee eacteeaget eeetgtattg 1686
atataacetg teaggetgge ttggttaggt tttactgggg eagaggatag ggaatetett 1746
attaaaacta acatgaaata tgtgttgttt teatttgeaa atttaaataa agatacataa 1806
tgtttgtatg

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15

<211> 395

<212> PRT

20 <213> Homo sapiens

<400> 121

Met Ser Gly Met Glu Glu Tyr Thr Thr Val Ser Gly Glu Val Leu Gln

1 5 10 15

25 Arg Trp Lys Ile Pro Ser Phe Lys Glu Asn Gln Thr Leu Ser Met Gly

|    |     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Ala | Ala | Thr | Val | Gln | Ser | Arg | Gly | Gln | Tyr | Ser | Cys | Ser | Gly | Gln | Val |
|    |     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
|    | Met | Tyr | Ile | Pro | Gln | Thr | Phe | Thr | Gln | Thr | Ser | Glu | Thr | Ala | Met | Val |
| 5  |     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
|    | Gln | Val | Gln | Glu | Leu | Phe | Pro | Pro | Pro | Val | Leu | Ser | Ala | Ile | Pro | Ser |
|    | 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
|    | Pro | Glu | Pro | Arg | Glu | Gly | Ser | Leu | Val | Thr | Leu | Arg | Cys | Gln | Thr | Lys |
|    |     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
| 10 | Leu | His | Pro | Leu | Arg | Ser | Ala | Leu | Arg | Leu | Leu | Phe | Ser | Phe | His | Lys |
|    |     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     | ė   |
|    | Asp | Gly | His | Thr | Leu | Gln | Asp | Arg | Gly | Pro | His | Pro | Glu | Leu | Cys | Ile |
|    |     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
|    | Pro | Gly | Ala | Lys | Glu | Gly | Asp | Ser | Gly | Leu | Tyr | Trp | Cys | Glu | Val | Ala |
| 15 |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
|    | Pro | Glu | Gly | Gly | Gln | Val | Gln | Lys | Gln | Ser | Pro | Gln | Leu | Glu | Val | Arg |
|    | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
|    | Val | Gln | Ala | Pro | Val | Ser | Arg | Pro | Val | Leu | Thr | Leu | His | His | Gly | Pro |
|    |     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
| 20 | Ala | Asp | Pro | Ala | Val | Gly | Asp | Met | Val | Gln | Leu | Leu | Cys | Glu | Ala | Gln |
|    |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
|    | Arg | Gly | Ser | Pro | Pro | Ile | Leu | Tyr | Ser | Phe | Tyr | Leu | Asp | Glu | Lys | Ile |
|    |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
|    | Val | Gly | Asn | His | Ser | Ala | Pro | Cys | Gly | Gly | Thr | Thr | Ser | Leu | Leu | Phe |
| 25 |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |

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|    | Pro | Val | Lys | Ser | Glu | Gln | Asp | Ala | Gly | Asn | Tyr | Ser | Cys | Glu | Ala | Glu |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
|    | Asn | Ser | ۷al | Ser | Arg | Glu | Arg | Ser | Glu | Pro | Lys | Lys | Leu | Ser | Leu | Lys |
|    |     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |
| 5  | Gly | Ser | Gln | Val | Leu | Phe | Thr | Pro | Ala | Ser | Asn | Trp | Leu | Val | Pro | Trp |
|    |     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |
|    | Leu | Pro | Ala | Ser | Leu | Leu | Gly | Leu | Met | Val | Ile | Ala | Ala | Ala | Leu | Leu |
|    |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |
|    | Val | Tyr | Val | Arg | Ser | Trp | Arg | Lys | Ala | Gly | Pro | Leu | Pro | Ser | Gln | Ile |
| 10 |     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |
|    | Pro | Pro | Thr | Ala | Pro | Gly | Gly | Glu | Gln | Cys | Pro | Leu | Tyr | Ala | Asn | Val |
|    | 305 |     |     |     |     | 310 |     |     | •   |     | 315 |     |     |     |     | 320 |
|    | His | His | Gln | Lys | Gly | Lys | Asp | Glu | Gly | Val | Val | Tyr | Ser | Val | Val | His |
|    |     |     |     |     | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |
| 15 | Arg | Thr | Ser | Lys | Arg | Ser | Glu | Ala | Arg | Ser | Ala | Glu | Phe | Thr | Val | Gly |
|    |     | •   |     | 340 |     |     |     |     | 345 |     |     | •   |     | 350 |     |     |
|    | Arg | Lys | Asp | Ser | Ser | Ile | Ile | Cys | Ala | Glu | Val | Arg | Cys | Leu | Gln | Pro |
|    |     |     | 355 |     |     |     |     | 360 |     | •   |     |     | 365 |     |     |     |
|    | Ser | Glu | Val | Ser | Ser | Thr | Glu | Val | Asn | Met | Arg | Ser | Arg | Thr | Leu | Gln |
| 20 |     | 370 | •   |     |     |     | 375 |     |     |     |     | 380 |     |     |     |     |
|    | Glu | Pro | Leu | Ser | Asp | Cys | Glu | Glu | Val | Leu | Cys |     |     |     |     |     |
|    | 385 |     |     |     |     | 390 |     |     |     |     | 395 |     |     |     |     |     |
|    |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |

<210> 122

25 <211> 550

### 275/346

<212> PRT

<213> Homo sapiens

|    | <400 | 0> 12 | 22  |     |     |     |     |     |     |     |      |     |     |     |     |     |
|----|------|-------|-----|-----|-----|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|
| 5  | Met  | Ala   | Phe | Ser | Lys | Leu | Leu | Glu | Gln | Ala | Gly  | Gly | Val | Gly | Leu | Phe |
|    | 1    |       |     |     | 5   |     |     |     |     | 10  |      |     |     |     | 15  |     |
|    | Gln  | Thr   | Leu | Gln | Val | Leu | Thr | Phe | Ile | Leu | Pro  | Cys | Leu | Met | Ile | Pro |
|    |      |       |     | 20  |     |     |     |     | 25  |     |      |     |     | 30  |     |     |
|    | Ser  | Gln   | Met | Leu | Leu | Glu | Asn | Phe | Ser | Ala | Ala  | Ile | Pro | Gly | His | Arg |
| 10 |      |       | 35  |     |     |     |     | 40  |     |     |      |     | 45  |     |     |     |
|    | Cys  | Trp   | Thr | His | Met | Leu | Asp | Asn | Gly | Ser | Ala  | Val | Ser | Thr | Asn | Met |
|    |      | 50    |     |     |     |     | 55  |     |     |     |      | 60  |     |     |     |     |
|    | Thr  | Pro   | Lys | Ala | Leu | Leu | Thr | Ile | Ser | Ile | Pro  | Pro | Gly | Pro | Asn | Gln |
|    | 65   |       |     |     |     | 70  |     |     |     |     | 75   |     |     |     |     | 80  |
| 15 | Gly  | Pro   | His | Gln | Cys | Arg | Arg | Phe | Arg | Gln | Pro  | Gln | Trp | Gln | Leu | Leu |
|    |      |       |     |     | 85  |     |     |     |     | 90  |      |     |     |     | 95  |     |
|    | Asp  | Pro   | Asn | Ala | Thr | Ala | Thr | Ser | Trp | Ser | Glu  | Ala | Asp | Thr | Glu | Pro |
|    |      |       |     | 100 |     |     |     |     | 105 |     |      |     |     | 110 |     |     |
|    | Cys  | Val   | Asp | Gly | Trp | Val | Tyr | Asp | Arg | Ser | Val  | Phe | Thr | Ser | Thr | Ile |
| 20 |      |       | 115 |     |     |     |     | 120 |     |     |      |     | 125 |     |     |     |
|    | Val  | Ala   | Lys | Trp | Asp | Leu | Val | Cys | Ser | Ser | Gln  | Gly | Leu | Lys | Pro | Leu |
|    |      | 130   |     |     |     |     | 135 |     |     |     |      | 140 |     |     |     |     |
|    | Ser  | Gln   | Ser | Ile | Phe | Met | Ser | Gly | Ile | Leu | Val. | Gly | Ser | Phe | Ile | Trp |
|    | 145  |       |     |     |     | 150 |     |     |     |     | 155  |     |     |     |     | 160 |
| 25 | Gly  | Leu   | Leu | Ser | Tyr | Arg | Phe | Gly | Arg | Lys | Pro  | Met | Leu | ser | Trp | Cys |

|    |     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Cys | Leu | Gln | Leu | Ala | Val | Ala | Gly | Thr | Ser | Thr | Ile | Phe | Ala | Pro | Thr |
|    |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
|    | Phe | Val | Ile | Tyr | Суѕ | Gly | Leu | Arg | Phe | Val | Ala | Ala | Phe | Gly | Met | Ala |
| 5  |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
|    | Gly | Ile | Phe | Leu | Ser | Ser | Leu | Thr | Leu | Met | Val | Glu | Trp | Thr | Thr | Thr |
|    |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
|    | Ser | Arg | Arg | Ala | Val | Thr | Met | Thr | Val | Val | Gly | Cys | Ala | Phe | Ser | Ala |
|    | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
| 10 | Gly | Gln | Ala | Ala | Leu | Gly | Gly | Leu | Ala | Phe | Ala | Leu | Arg | Asp | Trp | Arg |
|    |     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |
|    | Thr | Leu | Gln | Leu | Ala | Ala | Ser | Val | Pro | Phe | Phe | Ala | Ile | Ser | Leu | Ile |
|    |     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |
|    | Ser | Trp | Trp | Leu | Pro | Glu | Ser | Ala | Arg | Trp | Leu | Ile | Ile | Lys | Gly | Lys |
| 15 |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |
|    | Pro | Asp | Gln | Ala | Leu | Gln | Glu | Leu | Arg | Lys | Val | Ala | Arg | Ile | Asn | Gly |
|    |     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |
|    | His | Lys | Glu | Ala | Lys | Asn | Leu | Thr | Ile | Glu | Val | Leu | Met | Ser | Ser | Val |
|    | 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |
| 20 | Lys | Glu | Glu | Val | Ala | Ser | Ala | Lys | Glu | Pro | Arg | Ser | Val | Leu | Asp | Leu |
|    |     |     |     |     | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |
|    | Phe | Cys | Val | Pro | Val | Leu | Arg | Trp | Arg | Ser | Cys | Ala | Met | Leu | Val | Val |
|    |     |     |     | 340 |     |     |     |     | 345 |     |     |     |     | 350 |     |     |
|    | Asn | Phe | Ser | Leu | Leu | Ile | Ser | Tyr | Tyr | Gly | Leu | Val | Phe | Asp | Leu | Gln |
| 25 |     |     | 355 |     |     |     |     | 360 |     | -   |     |     | 365 |     |     |     |

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|    | Ser | Leu | Gly | Arg | Asp | Ile | Phe | Leu | Leu | Gln | Ala | Leu | Phe | Gly | Ala | Val |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    |     | 370 |     |     |     |     | 375 |     |     |     |     | 380 |     |     |     |     |
|    | Asp | Phe | Leu | Gly | Arg | Ala | Thr | Thr | Ala | Leu | Leu | Leu | Ser | Phe | Leu | Gly |
|    | 385 |     |     |     |     | 390 |     |     |     |     | 395 |     |     |     |     | 400 |
| 5  | Arg | Arg | Thr | Ile | Gln | Ala | Gly | Ser | Gln | Ala | Met | Ala | Gly | Leu | Ala | Ile |
|    |     |     |     |     | 405 |     |     |     |     | 410 |     |     |     |     | 415 |     |
|    | Leu | Ala | Asn | Met | Leu | Val | Pro | Gln | Asp | Leu | Gln | Thr | Leu | Arg | Val | Val |
|    |     |     |     | 420 |     |     |     |     | 425 |     |     |     |     | 430 |     |     |
|    | Phe | Ala | Val | Leu | Gly | Lys | Gly | Cys | Phe | Gly | Ile | Ser | Leu | Thr | Cys | Leu |
| 10 |     |     | 435 |     |     |     |     | 440 |     |     |     |     | 445 |     |     |     |
|    | Thr | Ile | Tyr | Lys | Ala | Glu | Leu | Phe | Pro | Thr | Pro | Val | Arg | Met | Thr | Ala |
|    |     | 450 |     |     |     |     | 455 |     |     |     |     | 460 |     |     |     |     |
|    |     |     |     |     |     |     | •   |     |     |     |     |     |     |     |     |     |
|    | Asp | Gly | Ile | Leu | His | Thr | Val | Gly | Arg | Leu | Gly | Ala | Met | Met | Gly | Pro |
|    | 465 |     |     |     |     | 470 |     |     |     |     | 475 |     |     |     |     | 480 |
| 15 | Leu | Ile | Leu | Met | Ser | Arg | Gln | Ala | Leu | Pro | Leu | Leu | Pro | Pro | Leu | Leu |
|    |     |     |     |     | 485 |     |     |     |     | 490 |     |     |     |     | 495 |     |
|    | Tyr | Gly | Val | Ile | Ser | Ile | Ala | Ser | Ser | Leu | Val | Val | Leu | Phe | Phe | Leu |
|    |     |     |     | 500 |     |     |     |     | 505 |     |     |     |     | 510 |     |     |
|    | Pro | Glu | Thr | Gln | Gly | Leu | Pro | Leu | Pro | Asp | Thr | Ile | Gln | Asp | Leu | Glu |
| 20 |     |     | 515 |     |     |     |     | 520 |     |     |     |     | 525 |     |     |     |
|    | Ser | Gln | Lys | Ser | Thr | Ala | Ala | Gln | Gly | Asn | Arg | Gln | Glu | Ala | Val | Thr |
|    |     | 530 |     |     |     |     | 535 |     |     |     |     | 540 |     |     |     |     |
|    | Val | Glu | Ser | Thr | Ser | Leu |     |     |     |     |     |     |     |     |     |     |
|    | 545 |     |     |     |     | 550 |     |     |     |     |     |     |     |     |     |     |

25

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|    | <21 | 0> 1  | 23    |      |     |     |     |     |      |      |     |             |       |                      |     |     |
|----|-----|-------|-------|------|-----|-----|-----|-----|------|------|-----|-------------|-------|----------------------|-----|-----|
|    | <21 | 1> 2  | 18    |      |     |     |     |     |      | ,    |     |             |       |                      |     |     |
|    | <21 | 2> P  | RT    |      |     |     |     |     |      |      |     |             |       |                      |     |     |
|    | <21 | 3> H  | omo : | sapi | ens |     |     |     |      |      |     |             |       |                      |     |     |
| 5  |     |       |       |      |     |     |     |     |      |      |     |             |       |                      |     |     |
|    | <40 | 0> 1: | 23    |      |     |     |     |     |      |      |     |             |       |                      |     |     |
|    | Met | Lys   | His   | Thr  | Leu | Ala | Leu | Leu | Ala  | Pro  | Leu | Leu         | Gly   | Leu                  | Gly | Let |
|    | 1   |       |       |      | 5   |     |     |     |      | 10   |     |             |       |                      | 15  |     |
|    | Gly | Leu   | Ala   | Leu  | Ser | Gln | Leu | Ala | Ala  | Gly  | Ala | Thr         | Asp   | Cys                  | Lys | Phe |
| 10 |     |       |       | 20   |     |     |     |     | 25   |      |     |             |       | 30                   |     |     |
|    | Leu | Gly   | Pro   | Ala  | Glu | His | Leu | Thr | Phe  | Thr  | Pro | Ala         | Ala   | Arg                  | Ala | Arg |
|    |     |       | 35    |      |     |     |     | 40  |      |      |     |             | 45    |                      |     |     |
|    | Trp | Leu   | Ala   | Pro  | Arg | Val | Arg | Ala | Pro  | Gly  | Leu | Leu         | Asp   | Ser                  | Leu | Tvr |
|    |     | 50    |       |      |     |     | 55  |     |      | _    |     | 60          | •     |                      |     | -3- |
| 15 | Gly | Thr   | Val   | Ara  | Ara | Phe |     | Ser | Val  | Val  | Gln |             | Asn   | Pro                  | Phe | Pro |
|    | 65  |       |       |      | 5   | 70  |     |     |      | ,,,, | 75  | acu.        | 11011 | 110                  | THE |     |
|    |     | Glu   | Len   | T-V  | Luc |     | Ton | Tou | 700  | C1   |     | <b>N1</b> - | 0     | <b>**</b> - <b>1</b> | •   | 80  |
|    | DCI | JIU   | Leu   | VAI  |     | AIa | пеп | теп | ASII |      | ьeu | AIa         | ser   | vaı                  | -   | vaı |
| •  |     | 21    | 1     |      | 85  |     |     |     |      | 90   |     |             |       |                      | 95  |     |
|    | Asn | GIU   | Val   |      | Arg | Tyr | Glu | Ala | Gly  | Tyr  | Val | Val         | Cys   | Ala                  | Val | Ile |
| 20 |     |       |       | 100  |     |     |     |     | 105  |      |     |             |       | 110                  |     |     |
|    | Ala | Gly   | Leu   | Tyr  | Leu | Leu | Leu | Val | Pro  | Thr  | Ala | Gly         | Leu   | Cys                  | Phe | Cys |
|    |     |       | 115   |      |     |     |     | 120 |      |      |     |             | 125   |                      |     |     |
|    | Cys | Cys   | Arg   | Cys  | His | Arg | Arg | Cys | Gly  | Gly  | Arg | Val         | Lys   | Thr                  | Gļu | His |
|    |     | 130   |       |      |     |     | 135 |     |      |      |     | 140         |       |                      |     |     |
| 25 | Lys | Ala   | Leu   | Ala  | Cys | Glu | Arg | Ala | Ala  | Leu  | Met | Val         | Phe   | Leu                  | Leu | Leu |

|    | 145 |       |       |       |       | 150   |       |       |       |     | 155   |       |       |       |       | 160   |
|----|-----|-------|-------|-------|-------|-------|-------|-------|-------|-----|-------|-------|-------|-------|-------|-------|
|    | Thr | Thr   | Leu   | Leu   | Leu   | Leu   | Ile   | Gly   | Val   | Val | Cys   | Ala   | Phe   | Val   | Thr   | Asn   |
|    |     |       |       |       | 165   |       |       |       |       | 170 |       |       |       |       | 175   |       |
|    | Gln | Arg   | Thr   | His   | Glu   | Gln   | Met   | Gly   | Pro   | Ser | Ile   | Glu   | Ala   | Met   | Pro   | Glu   |
| 5  |     |       |       | 180   |       |       |       |       | 185   |     |       |       |       | 190   |       |       |
|    | Thr | Leu   | Leu   | Ser   | Leu   | Trp   | Gly   | Leu   | Val   | Ser | Asp   | Val   | Pro   | Gln   | Val   | Ser   |
|    |     |       | 195   |       |       |       |       | 200   |       |     |       |       | 205   |       |       |       |
|    | Thr | Val   | Thr   | Pro   | His   | Pro   | His   | Val   | Pro   | Leu |       |       |       |       |       |       |
|    |     | 210   |       |       |       |       | 215   |       |       |     |       |       |       |       |       |       |
| 10 |     |       |       |       |       |       |       |       |       |     |       |       |       |       |       |       |
|    | <21 | 0> 1: | 24    |       |       |       |       |       |       |     |       |       |       |       |       |       |
|    | <21 | 1> 5  | 96    |       |       |       |       |       |       |     |       |       |       |       |       |       |
|    | <21 | 2> P  | RT    |       |       |       |       |       |       |     |       |       |       |       |       |       |
|    | <21 | 3> H  | omo   | sapi  | ens   |       |       |       |       |     |       |       |       |       |       |       |
| 15 |     |       |       |       |       |       |       |       |       |     |       |       |       |       |       |       |
|    | <40 | 0> 1  | 24    |       |       |       | •     |       |       |     |       |       |       |       |       |       |
|    | Met | Ala   | Ala   | Asn   | Ser   | Thr   | Ser   | Asp   | Leu   | His | Thr   | Pro   | Gly   | Thr   | Gln   | Leu   |
|    | 1   |       |       |       | 5     |       |       |       |       | 10  |       |       |       |       | 15    |       |
|    | Ser | · Val | Ala   | Asp   | Ile   | Ile   | val   | Ile   | Thr   | Val | . Tyr | Phe   | Ala   | Leu   | Asn   | Val   |
| 20 |     |       |       | 20    |       |       |       |       | 25    |     |       |       |       | 30    |       |       |
|    | Ala | val   | . Gly | 7 Ile | Trp   | Ser   | Ser   | Cys   | Arg   | Ala | Ser   | Arg   | Asr   | 1 Thr | · Val | Asr   |
|    |     |       | 35    |       |       |       |       | 40    |       |     |       |       | 45    |       |       |       |
|    | Gly | у Туг | Phe   | e Leu | ı Ala | Gly   |       |       | Met   | Thi | : Trp |       |       | ) Ile | : Gl  | Ala   |
|    |     | 50    |       |       |       |       | 55    |       |       |     |       | 60    |       |       |       |       |
| 25 | Sei | Let   | ı Phe | e Ala | a Sei | : Sei | c Gli | ı Gly | , Sei | Gly | y Lev | ı Phe | e Ile | e Gly | Let   | ı Ala |

|      | 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|      | Gly | Ser | Gly | Ala | Ala | Gly | Gly | Leu | Ala | Val | Ala | Gly | Phe | Glu | Trp | Asn |
|      |     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
|      | Ala | Thr | Tyr | Val | Leu | Leu | Ala | Leu | Ala | Trp | Val | Phe | Val | Pro | Ile | Tyr |
| 5    |     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
|      | Ile | Ser | Ser | Glu | Ile | Val | Thr | Leu | Pro | Glu | Tyr | Ile | Gln | Lys | Arg | Tyr |
|      |     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
|      | Gly | Gly | Gln | Arg | Ile | Arg | Met | Tyr | Leu | Ser | Val | Leu | Ser | Leu | Leu | Leu |
|      |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
| 10 · | Ser | Val | Phe | Thr | Lys | Ile | Ser | Leu | Asp | Leu | Tyr | Ala | Gly | Ala | Leu | Phe |
|      | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
|      | Val | His | Ile | Cys | Leu | Gly | Trp | Asn | Phe | Tyr | Leu | Ser | Thr | Ile | Leu | Thr |
|      |     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
|      | Leu | Gly | Ile | Thr | Ala | Leu | Tyr | Thr | Ile | Ala | Gly | Gly | Leu | Ala | Ala | Val |
| 15   |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
|      | Ile | Tyr | Thr | Asp | Ala | Leu | Gln | Thr | Leu | Ile | Met | Val | Val | Gly | Ala | Val |
|      |     |     | 195 |     |     |     |     | 200 |     | •   |     |     | 205 |     |     |     |
|      | Ile | Leu | Thr | Ile | Lys | Ala | Phe | Asp | Gln | Ile | Gly | Gly | Tyr | Gly | Gln | Leu |
|      |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
| 20   | Glu | Ala | Ala | Tyr | Ala | Gln | Ala | Ile | Pro | Ser | Arg | Thr | Ile | Ala | Asn | Thr |
|      | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
|      | Thr | Cys | His | Leu | Pro | Arg | Thr | Asp | Ala | Met | His | Met | Phe | Arg | Asp | Pro |
|      |     |     |     |     | 245 |     |     |     | •   | 250 |     |     |     |     | 255 |     |
|      | His | Thr | Gly | Asp | Leu | Pro | Trp | Thr | Gly | Met | Thr | Phe | Gly | Leu | Thr | Ile |
| 25   |     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |

|   |    | Met | Ala | Thr | Trp | Tyr | Trp | Cys | Thr | Asp | Gln | Val | Ile | Val | Gln | Arg | Ser |
|---|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|   |    |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |
|   |    | Leu | Ser | Ala | Arg | Asp | Leu | Asn | His | Ala | Lys | Ala | Gly | Ser | Ile | Leu | Ala |
|   |    |     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |
|   | 5  | Ser | Tyr | Leu | Lys | Met | Leu | Pro | Met | Gly | Leu | Ile | Ile | Met | Pro | Gly | Met |
|   |    | 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |
|   |    | Ile | Ser | Arg | Ala | Leu | Phe | Pro | Asp | Asp | Val | Gly | Cys | Val | Val | Pro | Ser |
|   |    |     |     |     |     | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |
|   |    | Glu | Cys | Leu | Arg | Ala | Cys | Gly | Ala | Glu | Val | Gly | Cys | Ser | Asn | Ile | Ala |
| 1 | .0 |     |     |     | 340 |     |     |     |     | 345 | •   |     |     |     | 350 |     |     |
|   |    | Tyr | Pro | Lys | Leu | Val | Met | Glu | Leu | Met | Pro | Ile | Gly | Leu | Arg | Gly | Leu |
|   |    |     |     | 355 |     |     | ٠   |     | 360 |     |     |     |     | 365 |     |     |     |
|   |    | Met | Ile | Ala | Val | Met | Leu | Ala | Ala | Leu | Met | Ser | Ser | Leu | Thr | Ser | Ile |
|   |    |     | 370 |     |     |     |     | 375 |     |     |     |     | 380 |     |     |     |     |
| 1 | .5 | Phe | Asn | Ser | Ser | Ser | Thr | Leu | Phe | Thr | Met | Asp | Ile | Trp | Arg | Arg | Leu |
|   |    | 385 |     |     |     |     | 390 |     |     |     |     | 395 |     |     |     |     | 400 |
|   |    | Arg | Pro | Arg | Ser | Gly | Glu | Arg | Glu | Leu | Leu | Leu | Val | Gly | Arg | Leu | Val |
|   |    |     |     |     |     | 405 |     |     |     |     | 410 |     |     |     |     | 415 | _   |
|   |    | Ile | Val | Ala | Leu | Ile | Gly | Val | Ser | Val | Ala | Trp | Ile | Pro | Val | Leu | Gln |
| 2 | 20 |     |     |     | 420 |     |     |     |     | 425 |     |     |     |     | 430 |     |     |
|   |    | Asp | Ser | Asn | Ser | Gly | Gln | Leu | Phe | Ile | Tyr | Met | Gln | Ser | Val | Thr | Ser |
|   |    |     |     | 435 |     |     |     |     | 440 |     |     |     |     | 445 |     |     |     |
|   |    | Ser | Leu | Ala | Pro | Pro | Val | Thr | Ala | Val | Phe | Val | Leu | Gly | Val | Phe | Trp |
|   |    |     | 450 |     |     |     |     | 455 |     |     |     |     | 460 |     |     |     |     |
| 2 | 25 | Arg | Arg | Ala | Asn | Glu | Gln | Gly | Ala | Phe | Trp | Gly | Leu | Ile | Ala | Gly | Leu |

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Val Val Gly Ala Thr Arg Leu Val Leu Glu Phe Leu Asn Pro Ala Pro Pro Cys Gly Glu Pro Asp Thr Arg Pro Ala Val Leu Gly Ser Ile His Tyr Leu His Phe Ala Val Ala Leu Phe Ala Leu Ser Gly Ala Val Val Val Ala Gly Ser Leu Leu Thr Pro Pro Pro Gln Ser Val Gln Ile Glu Asn Leu Thr Trp Trp Thr Leu Ala Gln Asp Val Pro Leu Gly Thr Lys Ala Gly Asp Gly Gln Thr Pro Gln Lys His Ala Phe Trp Ala Arg Val Cys Gly Phe Asn Ala Ile Leu Leu Met Cys Val Asn Ile Phe Tyr Ala Tyr Phe Ala <210> 125 <211> 467 <212> PRT <213> Homo sapiens <400> 125

Met Trp Arg Cys Pro Leu Gly Leu Leu Leu Leu Pro Leu Ala Gly

|     | 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|     | His | Leu | Ala | Leu | Gly | Ala | Gln | Gln | Gly | Arg | Gly | Arg | Arg | Glu | Leu | Ala |
|     |     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
|     | Pro | Gly | Leu | His | Leu | Arg | Gly | Ile | Arg | Asp | Ala | Gly | Gly | Arg | Tyr | Cys |
| 5   |     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
|     | Gln | Glu | Gln | Asp | Leu | Cys | Cys | Arg | Gly | Arg | Ala | Asp | Asp | Cys | Ala | Leu |
|     |     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
|     | Pro | Tyr | Leu | Gly | Ala | Ile | Суѕ | Tyr | Cys | Asp | Leu | Phe | Cys | Asn | Arg | Thr |
|     | 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
| LO  | Val | Ser | Asp | Cys | Cys | Pro | Asp | Phe | Trp | Asp | Phe | Cys | Leu | Gly | Val | Pro |
|     |     | •   |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
|     | Pro | Pro | Phe | Pro | Pro | Ile | Gln | Gly | Cys | Met | His | Gly | Gly | Arg | Ile | Tyr |
|     |     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
|     | Pro | Val | Leu | Gly | Thr | Tyr | Trp | Asp | Asn | Cys | Asn | Arg | Cys | Thr | Cys | Gln |
| 1.5 |     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
|     | Glu | Asn | Arg | Gln | Trp | Gln | Cys | Asp | Gln | Glu | Pro | Cys | Leu | Val | Asp | Pro |
|     |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
|     | Asp | Met | Ile | Lys | Ala | Ile | Asn | Gln | Gly | Asn | Tyr | Gly | Trp | Gln | Ala | Gly |
|     | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
| 20  | Asn | His | Ser | Ala | Phe | Trp | Gly | Met | Thr | Leu | Asp | Glu | Gly | Ile | Arg | Tyr |
|     |     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
|     | Arg | Leu | Gly | Thr | Ile | Arg | Pro | Ser | Ser | Ser | Val | Met | Asn | Met | His | Glu |
|     |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
|     | Ile | Tyr | Thr | Val | Leu | Asn | Pro | Gly | Glu | Val | Leu | Pro | Thr | Ala | Phe | Glu |
| 25  |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |

|    | Ala | Ser | Glu | Lys | Trp | Pro | Asn | Leu | Ile | His | Glu | Pro | Leu | Asp | Gln | Gly |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
|    | Asn | Cys | Ala | Gly | Ser | Trp | Ala | Phe | Ser | Thr | Ala | Ala | Val | Ala | Ser | Asp |
|    | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
| 5  | Arg | Val | Ser | Ile | His | Ser | Leu | Gly | His | Met | Thr | Pro | Val | Leu | Ser | Pro |
|    |     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |
|    | Gln | Asn | Leu | Leu | Ser | Cys | Asp | Thr | His | Gln | Gln | Gln | Gly | Cys | Arg | Gly |
|    |     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |
|    | Gly | Arg | Leu | Asp | Gly | Ala | Trp | Trp | Phe | Leu | Arg | Arg | Arg | Gly | Val | Val |
| 10 |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |
|    | Ser | Asp | His | Cys | Tyr | Pro | Phe | Ser | Gly | Arg | Glu | Arg | Asp | Glu | Ala | Gly |
|    |     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |
|    | Pro | Ala | Pro | Pro | Cys | Met | Met | His | Ser | Arg | Ala | Met | Gly | Arg | Gly | Lys |
|    | 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |
| 15 | Arg | Gln | Ala | Thr | Ala | His | Cys | Pro | Asn | Ser | Tyr | Val | Asn | Asn | Asn | Asp |
|    |     |     | ÷   |     | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |
|    | Ile | Tyr | Gln | Val | Thr | Pro | Val | Tyr | Arg | Leu | Gly | Ser | Asn | Asp | Lys | Glu |
|    |     |     |     | 340 |     |     |     |     | 345 |     |     |     |     | 350 |     |     |
|    | Ile | Met | Lys | Glu | Leu | Met | Glu | Asn | Gly | Pro | Val | Gln | Ala | Leu | Met | Glu |
| 20 |     |     | 355 |     |     |     |     | 360 |     |     |     |     | 365 |     |     |     |
|    | Val | His | Glu | Asp | Phe | Phe | Leu | Tyr | Lys | Gly | Gly | Ile | Tyr | Ser | His | Thr |
|    |     | 370 |     |     |     |     | 375 |     |     |     |     | 380 |     |     |     |     |
|    | Pro | Val | Ser | Leu | Gly | Arg | Pro | Glu | Arg | Tyr | Arg | Arg | His | Gly | Thr | His |
|    | 385 |     |     |     |     | 390 |     |     |     |     | 395 |     |     |     |     | 400 |
| 25 | Ser | Val | Lys | Ile | Thr | Gly | Trp | Glv | Glu | Glu | Thr | Leu | Pro | asp | Glv | Ara |

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Thr Leu Lys Tyr Trp Thr Ala Ala Asn Ser Trp Gly Pro Ala Trp Gly Glu Arg Gly His Phe Arg Ile Val Arg Gly Val Asn Glu Cys Asp Ile Glu Ser Phe Val Leu Gly Val Trp Gly Arg Val Gly Met Glu Asp Met Gly His His <210> 126 <211> 476 <212> PRT <213> Homo sapiens <400> 126 Met Ala Gly Ser Asp Thr Ala Pro Phe Leu Ser Gln Ala Asp Asp Pro Asp Asp Gly Pro Val Pro Gly Thr Pro Gly Leu Pro Gly Ser Thr Gly Asn Pro Lys Ser Glu Glu Pro Glu Val Pro Asp Gln Glu Gly Leu Gln Arg Ile Thr Gly Leu Ser Pro Gly Arg Ser Ala Leu Ile Val Ala Val Leu Cys Tyr Ile Asn Leu Leu Asn Tyr Met Asp Arg Phe Thr Val Ala

|    | 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Gly | Val | Leu | Pro | Asp | Ile | Glu | Gln | Phe | Phe | Asn | Ile | Gly | Asp | Ser | Ser |
|    |     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
|    | Ser | Gly | Leu | Ile | Gln | Thr | Val | Phe | Ile | Ser | Ser | Tyr | Met | Val | Leu | Ala |
| 5  |     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
|    | Pro | Val | Phe | Gly | Tyr | Leu | Gly | Asp | Arg | Tyr | Asn | Arg | Lys | Tyr | Leu | Met |
|    |     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
|    | Cys | Gly | Gly | Ile | Ala | Phe | Trp | Ser | Leu | Val | Thr | Leu | Gly | Ser | Ser | Phe |
|    |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
| 10 | Ile | Pro | Gly | Glu | His | Phe | Trp | Leu | Leu | Leu | Leu | Thr | Arg | Gly | Leu | Val |
|    | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
|    | Gly | Val | Gly | Glu | Ala | Ser | Tyr | Ser | Thr | Ile | Ala | Pro | Thr | Leu | Ile | Ala |
|    |     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
|    | Asp | Leu | Phe | Val | Ala | Asp | Gln | Arg | Ser | Arg | Met | Leu | Ser | Ile | Phe | Tyr |
| 15 |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
|    | Phe | Ala | Ile | Pro | Val | Gly | Ser | Gly | Leu | Gly | Tyr | Ile | Ala | Gly | Ser | Lys |
|    |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
|    | Val | Lys | Asp | Met | Ala | Gly | Asp | Trp | His | Trp | Ala | Leu | Arg | Val | Thr | Pro |
|    |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
| 20 | Gly | Leu | Gly | Val | Val | Ala | Val | Leu | Leu | Leu | Phe | Leu | Val | Val | Arg | Glu |
|    | 225 |     |     |     |     | 230 |     |     |     | ,   | 235 |     |     |     |     | 240 |
|    | Pro | Pro | Arg | Gly | Ala | Val | Glu | Arg | His | Ser | Asp | Leu | Pro | Pro | Leu | Asn |
|    |     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |
|    | Pro | Thr | Ser | Trp | Trp | Ala | Asp | Leu | Arg | Ala | Leu | Ala | Arg | Asn | Leu | Ile |
| 25 |     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |

|    | Phe | Gly | Leu | Ile | Thr | Cys | Leu | Thr | Gly | Val | Leu | Gly | Val | Gly | Leu | Gl. |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |
|    | Val | Glu | Ile | Ser | Arg | Arg | Leu | Arg | His | Ser | Asn | Pro | Arg | Ala | Asp | Pro |
|    |     | 290 |     |     |     |     | 295 |     |     |     | •   | 300 |     |     |     |     |
| 5  | Leu | Val | Cys | Ala | Thr | Gly | Leu | Leu | Gly | Ser | Ala | Pro | Phe | Leu | Phe | Le  |
|    | 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |
|    | Ser | Leu | Ala | Cys | Ala | Arg | Gly | Ser | Ile | Val | Ala | Thr | Tyr | Ile | Phe | Ile |
|    |     |     |     |     | 325 |     |     |     | •   | 330 |     |     |     |     | 335 |     |
|    | Phe | Ile | Gly | Glu | Thr | Leu | Leu | Ser | Met | Asn | Trp | Ala | Ile | Val | Ala | Ası |
| 10 |     |     |     | 340 |     |     |     |     | 345 |     |     |     |     | 350 |     |     |
|    | Ile | Leu | Leu | Tyr | Val | Val | Ile | Pro | Thr | Arg | Arg | Ser | Thr | Ala | Glu | Ala |
|    |     |     | 355 |     |     |     |     | 360 |     |     |     |     | 365 |     |     |     |
|    | Phe | Gln | Ile | Val | Leu | Ser | His | Leu | Leu | Gly | Asp | Ala | Gly | Ser | Pro | Туг |
|    |     | 370 |     |     |     |     | 375 |     |     |     |     | 380 |     |     |     |     |
| 15 | Leu | Ile | Gly | Leu | Ile | Ser | Asp | Arg | Leu | Arg | Arg | Asn | Trp | Pro | Pro | Ser |
|    | 385 |     |     |     |     | 390 |     |     |     |     | 395 |     |     |     |     | 400 |
|    | Phe | Leu | Ser | Glu | Phe | Arg | Ala | Leu | Gln | Phe | Ser | Leu | Met | Leu | Cys | Ala |
|    |     |     |     |     | 405 |     |     |     |     | 410 |     |     |     |     | 415 |     |
|    | Phe | Val | Gly | Ala | Leu | Gly | Gly | Ala | Ala | Phe | Leu | Gly | Thr | Ala | Ile | Phe |
| 20 |     |     |     | 420 |     |     |     |     | 425 |     |     |     |     | 430 |     |     |
|    | Ile | Glu | Ala | Asp | Arg | Arg | Arg | Ala | Gln | Leu | His | Val | Gln | Gly | Leu | Leu |
|    |     |     | 435 |     |     |     |     | 440 |     |     |     |     | 445 |     |     |     |
|    | His | Glu | Ala | Gly | Ser | Thr | Asp | Asp | Arg | Ile | Val | Val | Pro | Gln | Arg | Gly |
|    |     | 450 |     |     |     |     | 455 |     |     |     |     | 460 |     |     |     |     |
| 25 | Arg | Ser | Thr | Arg | Val | Pro | Val | Ala | Ser | Val | Leu | Ile |     |     |     |     |

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<210> 127 <211> 449 <212> PRT <213> Homo sapiens <400> 127 Met Ser Asp Ile Arg His Ser Leu Leu Arg Arg Asp Ala Leu Ser Ala 5. Ala Lys Glu Val Leu Tyr His Leu Asp Ile Tyr Phe Ser Ser Gln Leu Gln Ser Ala Pro Leu Pro Ile Val Asp Lys Gly Pro Val Glu Leu Leu Glu Glu Phe Val Phe Gln Val Pro Lys Glu Arg Ser Ala Gln Pro Lys Arg Leu Asn Ser Leu Gln Glu Leu Gln Leu Leu Glu Ile Met Cys Asn Tyr Phe Gln Glu Gln Thr Lys Asp Ser Val Arg Gln Ile Ile Phe Ser Ser Leu Phe Ser Pro Gln Gly Asn Lys Ala Asp Asp Ser Arg Met Ser Leu Leu Gly Lys Leu Val Ser Met Ala Val Ala Val Cys Arg Ile Pro 

Val Leu Glu Cys Ala Ala Ser Trp Leu Gln Arg Thr Pro Val Val Tyr

|    |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |       |  |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------|--|
|    | Cys | Val | Arg | Leu | Ala | Lys | Ala | Leu | Val | Asp | Asp | Tyr | Cys | Cys | Leu | Val   |  |
|    | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160   |  |
|    | Pro | Gly | Ser | Ile | Gln | Thr | Leu | Lys | Gln | Ile | Phe | Ser | Ala | Ser | Pro | Arg ' |  |
| 5  |     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |       |  |
|    | Phe | Cys | Cys | Gln | Phe | Ile | Thr | Ser | Val | Thr | Ala | Leu | Tyr | Asp | Leu | Ser   |  |
|    |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |       |  |
|    | Ser | Asp | Asp | Leu | Ile | Pro | Pro | Met | Asp | Leu | Leu | Glu | Met | Ile | Val | Thr   |  |
|    |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |       |  |
| 10 | Trp | Ile | Phe | Glu | Asp | Pro | Arg | Leu | Ile | Leu | Ile | Thr | Phe | Leu | Asn | Thr   |  |
|    |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |       |  |
|    | Pro | Ile | Ala | Ala | Asn | Leu | Pro | Ile | Gly | Phe | Leu | Glu | Leu | Thr | Pro | Leu   |  |
|    | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240   |  |
|    | Val | Gly | Leu | Ile | Arg | Trp | Cys | Val | Lys | Ala | Pro | Leu | Ala | Tyr | Lys | Arg   |  |
| 15 |     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |       |  |
|    | Lys | Lys | Lys | Pro | Pro | Leu | Ser | Asn | Gly | His | Val | Ser | Asn | Lys | Val | Thr   |  |
|    |     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |       |  |
|    | Lys | Asp | Pro | Gly | Val | Gly | Met | Asp | Arg | Asp | Ser | His | Leu | Leu | Tyr | Ser   |  |
|    |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |       |  |
| 20 | Lys | Leu | His | Leu | Ser | Val | Leu | Gln | Val | Leu | Met | Thr | Leu | Gln | Leu | His   |  |
|    |     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |       |  |
|    | Leu | Thr | Glu | Lys | Asn | Leu | Tyr | Gly | Arg | Leu | Gly | Leu | Ile | Leu | Phe | Asp   |  |
|    | 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320   |  |
|    | His | Met | Val | Pro | Leu | Val | Glu | Glu | Ile | Asn | Arg | Leu | Ala | Asp | Glu | Leu   |  |
| 25 |     |     |     |     | 325 |     |     |     |     | 330 |     |     |     |     | 225 |       |  |

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Asn Pro Leu Asn Ala Ser Gln Glu Ile Glu Leu Ser Leu Asp Arg Leu Ala Gin Ala Leu Gin Val Ala Met Ala Ser Gly Ala Leu Leu Cys Thr Arg Asp Asp Leu Arg Thr Leu Cys Ser Arg Leu Pro His Asn Asn Leu Leu Gln Leu Val Ile Ser Gly Pro Val Gln Gln Ser Pro His Ala Ala Leu Pro Pro Gly Phe Tyr Pro His Ile His Thr Pro Pro Leu Gly Tyr ` 410 Gly Ala Val Pro Ala His Pro Ala Ala His Pro Ala Leu Pro Thr His Pro Gly His Thr Phe Ile Ser Gly Val Thr Phe Pro Phe Arg Pro Ile Arg <210> 128 <211> 105 <212> PRT <213> Homo sapiens <400> 128 Met Arg Arg Ile Ser Leu Thr Ser Ser Pro Val Arg Leu Leu Leu Phe

|    | Leu  | Leu   | Leu   | Leu   | Leu | Ile | Ala | Leu | Glu | Ile | Met | Val | Gly | Gly | His | Ser |
|----|------|-------|-------|-------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    |      |       |       | 20    |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
|    | Leu  | Cys   | Phe   | Asn   | Phe | Thr | Ile | Lys | Ser | Leu | Ser | Arg | Pro | Gly | Gln | Pro |
|    |      |       | 35    |       |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
| 5  | Trp  | Суз   | Glu   | Ala   | Gln | Val | Phe | Leu | Asn | Lys | Asn | Leu | Phe | Leu | Gln | Tyr |
|    |      | 50    |       |       |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
|    | Asn  | Ser   | Asp   | Asn   | Asn | Met | Val | Lys | Pro | Leu | Gly | Leu | Leu | Gly | Lys | Lys |
|    | 65   |       | ,     |       |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
|    | Val  | Asn   | Ala   | Thr   | Ser | Thr | Trp | Gly | Glu | Asn | Pro | Asn | Ala | Gly | Arg | Ser |
| 10 |      |       |       |       | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
|    | Gly  | Ala   | Arg   | Pro   | Gln | Asp | Ala | Pro | Leu |     |     |     |     |     |     |     |
|    |      |       |       | 100   |     |     |     |     | 105 |     |     |     |     |     |     |     |
|    |      |       |       |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <210 | )> 12 | 29    |       |     |     |     |     |     |     |     |     |     |     |     |     |
| 15 | <211 | l> 81 | L     |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <212 | ?> PF | T     |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <213 | 3> Ho | omo s | sapie | ens |     |     |     |     |     |     |     |     |     |     |     |
|    |      |       |       |       |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <400 | )> 12 | 29    |       |     |     |     |     |     |     |     |     |     |     |     |     |
| 20 | Met  | Ser   | Pro   | Asp   | Val | Arg | Phe | Leu | Pro | Leu |
|    | 1    |       |       |       | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
|    | Arg  | Arg   | Pro   | Val   | Pro | Val | Ala | Ala | Gly | Pro | Gly | Asp | Thr | Arg | Pro | Ala |
|    |      |       |       | 20    |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
|    | Leu  | Leu   | Ser   | Phe   | Glu | Ala | Pro | Val | Phe | Val | Pro | Thr | Leu | Thr | Pro | Gly |
| 25 |      |       | 35    |       |     |     |     | 40  |     |     |     |     | 45  |     |     |     |

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Cys Leu Gln Gln Pro Arg Gly Arg Asn Gly Ala Ser Pro Arg Gly Leu Leu Pro Gln Pro Leu Asp Gly Thr Ala Ala Ser Pro Val Cys His His Val <210> 130 <211> 552 <212> PRT <213> Homo sapiens <400> 130 Met Arg Arg Leu Thr Arg Arg Leu Val Leu Pro Val Phe Gly Val Leu Trp Ile Thr Val Leu Leu Phe Phe Trp Val Thr Lys Arg Lys Leu Glu Val Pro Thr Gly Pro Glu Val Gln Thr Pro Lys Pro Ser Asp Ala Asp Trp Asp Asp Leu Trp Asp Gln Phe Asp Glu Arg Arg Tyr Leu Asn Ala Lys Lys Trp Arg Val Gly Asp Asp Pro Tyr Lys Leu Tyr Ala Phe Asn Gln Arg Glu Ser Glu Arg Ile Ser Ser Asn Arg Ala Ile Pro Asp Thr

|    | Arg | His | Leu | Arg | Cys | Thr | Leu | Leu | Val | Tyr | Cys | Thr | Asp | Leu | Pro | Pro |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    |     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
|    | Thr | Ser | Ile | Ile | Ile | Thr | Phe | His | Asn | Glu | Ala | Arg | Ser | Thr | Leu | Leu |
|    |     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
| 5  | Arg | Thr | Ile | Arg | Ser | Val | Leu | Asn | Arg | Thr | Pro | Thr | His | Leu | Ile | Arg |
|    |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
|    | Glu | Ile | Ile | Leu | Val | Asp | Asp | Phe | Ser | Asn | Asp | Pro | Asp | Asp | Cys | Lys |
|    | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
|    | Gln | Leu | Ile | Lys | Leu | Pro | Lys | Val | Lys | Cys | Leu | Arg | Asn | Asn | Glu | Arg |
| 10 |     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
|    | Gln | Gly | Leu | Val | Arg | Ser | Arg | Ile | Arg | Gly | Ala | Asp | Ile | Ala | Gln | Gly |
|    |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
|    | Thr | Thr | Leu | Thr | Phe | Leu | Asp | Ser | His | Cys | Glu | Val | Asn | Arg | Asp | Trp |
|    |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
| 15 | Leu | Gln | Pro | Leu | Leu | His | Arg | Val | Lys | Glu | Asp | Tyr | Thr | Arg | Val | Val |
|    |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
|    | Cys | Pro | Val | Ile | Asp | Ile | Ile | Asn | Leu | Asp | Thr | Phe | Thr | Tyr | Ile | Glu |
|    | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
|    | Ser | Ala | Ser | Glu | Leu | Arg | Gly | Gly | Phe | Asp | Trp | Ser | Leu | His | Phe | Gln |
| 20 |     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |
|    | Trp | Glu | Gln | Leu | Ser | Pro | Glu | Gln | Lys | Ala | Arg | Arg | Leu | Asp | Pro | Thr |
|    |     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |
|    | Glu | Pro | Ile | Arg | Thr | Pro | Ile | Ile | Ala | Gly | Gly | Leu | Phe | Val | Ile | Asp |
|    |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |
| 25 | Lys | Ala | Trp | Phe | Asp | Tyr | Leu | Gly | Lys | Tyr | Asp | Met | Asp | Met | Asp | Ile |

|    |     | 290        |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |
|----|-----|------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Trp | Gly        | Gly | Glu | Asn | Phe | Glu | Ile | Ser | Phe | Arg | Val | Trp | Met | Суз | Gly |
|    | 305 |            |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |
|    | Gly | Ser        | Leu | Glu | Ile | Val | Pro | Cys | Ser | Arg | Val | Gly | His | Val | Phe | Arg |
| 5  |     |            |     |     | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |
|    | Lys | Lys        | His | Pro | Tyr | Val | Phe | Pro | Asp | Gly | Asn | Ala | Asn | Thr | Tyr | Ile |
|    |     |            |     | 340 |     |     |     |     | 345 |     |     |     |     | 350 |     |     |
|    | Lys | Asn        | Thr | Lys | Arg | Thr | Ala | Glu | Val | Trp | Met | Asp | Glu | Tyr | Lys | Gln |
|    |     |            | 355 |     |     |     |     | 360 |     |     |     |     | 365 |     |     |     |
| 10 | Tyr | Tyr        | Tyr | Ala | Ala | Arg | Pro | Phe | Ala | Leu | Glu | Arg | Pro | Phe | Gly | Asn |
|    |     | 370        |     |     |     |     | 375 |     |     |     |     | 380 |     |     |     |     |
|    | Val | Glu        | Ser | Arg | Leu | Asp | Leu | Arg | Lys | Asn | Leu | Arg | Cys | Gln | Ser | Phe |
|    | 385 |            |     |     |     | 390 |     |     |     |     | 395 |     |     |     |     | 400 |
|    | Lys | Trp        | Tyr | Leu | Glu | Asn | Ile | Tyr | Pro | Glu | Leu | Ser | Ile | Pro | Lys | Glu |
| 15 |     |            |     |     | 405 |     |     |     |     | 410 |     |     |     |     | 415 |     |
|    | Ser | Ser        | Ile | Gln | Lys | Gly | Asn | Ile | Arg | Gln | Arg | Gln | Lys | Cys | Leu | Glu |
|    |     |            |     | 420 |     |     |     |     | 425 |     |     |     |     | 430 |     |     |
|    | Ser | Gln        | Arg | Gln | Asn | Asn | Gln | Glu | Thr | Pro | Asn | Leu | Lys | Leu | Ser | Pro |
|    |     |            | 435 |     |     |     |     | 440 |     |     |     |     | 445 |     |     |     |
| 20 | Cys | Ala        | Lys | Val | Lys | Gly | Glu | Asp | Ala | Lys | Ser | Gln | Val | Trp | Ala | Phe |
|    |     | <b>450</b> |     |     |     |     | 455 |     |     |     |     | 460 |     |     |     |     |
|    | Thr | Tyr        | Thr | Gln | Gln | Ile | Leu | Gln | Glu | Glu | Leu | Cys | Leu | Ser | Val | Ile |
|    | 465 |            |     |     |     | 470 |     |     |     |     | 475 |     |     |     |     | 480 |
|    | Thr | Leu        | Phe | Pro | Gly | Ala | Pro | Val | Val | Leu | Val | Leu | Cys | Lys | Asn | Gly |
| 25 |     |            |     |     | 485 |     |     |     |     | 490 |     |     |     |     | 495 |     |

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Asp Asp Arg Gln Gln Trp Thr Lys Thr Gly Ser His Ile Glu His Ile
500 505 510

Ala Ser His Leu Cys Leu Asp Thr Asp Met Phe Gly Asp Gly Thr Glu
515 520 525

5 Asn Gly Lys Glu Ile Val Val Asn Pro Cys Glu Ser Ser Leu Met Ser 530 535 540

Gln His Trp Asp Met Val Ser Ser

545 550

10 <210> 131

<211> 1188

<212> DNA

<213> Homo sapiens

15 <400> 131

20

25

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#### 296/346

tecttetace ttgatgagaa gattgtgggg aaceaeteag etecetgtgg tggaaceaee 660

teceteetet teeeagtgaa gteagaacag gatgetggga aetaeteetg egaggetgag 720

aacagtgtet eeagagagag gagtgageee aagaagetgt etetgaaggg tteteaagte 780

ttgtteaete eegeeageaa etggetggtt eettggette etgegageet gettggeetg 840

atggttattg etgetgeaet tetggtttat gtgagateet ggagaaaage tgggeeeett 900

ceateeeaga taceaeeae ageteeaggt ggagageagt geeeaetata tgeeaaegtg 960

cateaeeaga aagggaaaga tgaaggtgtt gtetaeteetg tggtgeatag aaceteaaag 1020

aggagtgaag eeaggtetge tgagtteaee gtggggagaa aggaeagtte tateatetgt 1080

geggaggtga gatgeetgea geeeagtgag gttteateea eggaggtgaa tatgagaage 1140

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<210> 132

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20

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<211> 1653

<212> DNA

15 <213> Homo sapiens

<400> 132

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| ggcctcctct  | cctaccggtt | tgggaggaag | ccgatgctga | gctggtgctg | cctgcagttg | 540  |
|-------------|------------|------------|------------|------------|------------|------|
| gccgtggcgg  | gcaccagcac | catcttcgcc | ccaacattcg | tcatctactg | cggcctgcgg | 600  |
| ttcgtggccg  | cttttgggat | ggccggcatc | tttctgagtt | cactgacact | gatggtggag | 660  |
| tggaccacga  | ccagcaggag | ggcggtcacc | atgacggtgg | tgggatgtgc | cttcagcgca | 720  |
| ggccaggcgg  | cgctgggcgg | cctggccttt | gccctgcggg | actggaggac | tctccagctg | 780  |
| gcagcatcag  | tgcccttctt | tgccatctcc | ctgatatcct | ggtggctgcc | agaatccgcc | 840  |
| cggtggctga  | ttattaaggg | caaaccagac | caagcacttc | aggagctcag | aaaggtggcc | 900  |
| aggataaatg  | gccacaagga | ggccaagaac | ctgaccatag | aggtgctgat | gtccagcgtg | 960  |
| aaggaggagg  | tggcctctgc | aaaggagccg | cggtcggtgc | tggacctgtt | ctgcgtgccc | 1020 |
| gtgctccgct  | ggaggagctg | cgccatgctg | gtggtgaatt | tctctctatt | gatctcctac | 1080 |
| tatgggctgg  | tcttcgacct | gcagagcctg | ggccgtgaca | tcttcctcct | ccaggccctc | 1140 |
| ttcggggccg  | tggacttcct | gggccgggcc | accactgccc | tcttgctcag | tttccttggc | 1200 |
| cgccgcacca  | tccaggcggg | ttcccaggcc | atggccggcc | tcgccattct | agccaacatg | 1260 |
| ctggtgccgc  | aagatttgca | gaccctgcgt | gtggtctttg | ctgtgctggg | aaagggatgt | 1320 |
| tttgggataa  | gcctaacctg | cctcaccatc | tacaaggctg | aactctttcc | aacgccagtg | 1380 |
| cggatgacag  | cagatggcat | tctgcataca | gtgggccggc | tgggggctat | gatgggtccc | 1440 |
| 'ctgatcctga | tgagccgcca | agccctgccc | ctgctgcctc | ctctcctcta | tggcgttatc | 1500 |
| tccattgctt  | ccagcctggt | tgtgctgttc | ttcctcccgg | agacccaggg | acttccgctc | 1560 |
| cctgacacta  | tccaggacct | ggagagccag | aaatcaacag | cagcccaggg | caaccggcaa | 1620 |
| gaggccgtca  | ctgtggaaag | tacctcgctc | tag        |            |            | 1653 |

<210> 133

5

10

15

20

<211> 657

<212> DNA

25 <213> Homo sapiens

#### 298/346

<400> 133

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10

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ttcaccccag cagccagggc ccggtggctg gcccctcgag ttcgtgcgcc aggactcctg 180

gactccctct atggcaccgt gcgccgcttc ctctcggtgg tgcagctcaa tcctttccct 240

tcagagttgg taaaggccct actgaatgag ctggcctccg tgaaggtgaa tgaggtggtg 300

cggtacgagg cgggctacgt ggtatgcgct gtgatcgcgg gcctctacct gctgctggtg 360

cccactgccg ggctttgctt ctgctgctgc cgctgccacc ggcgctgcgg gggacgagtg 420

aagacagagc acaaggcgct ggcctgtgag cgcgcggccc tcatggtctt cctgctgctg 480

accaccctct tgctgctgat tggtgtggtc tgtgcctttg tcaccaacca gcgcacgcat 540

gaacagatgg gccccagcat cgaggccatg cctgagaccc tgctcagcct ctggggcctg 600

gtctctgatg tcccccaagt gagcactgtt acccctcacc ctcatgtgcc cctgtga 657

15 <210> 134

<211> 1791

<212> DNA

<213> Homo sapiens

20 <400> 134

25

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|   | ctgctggcac | tggcatgggt | gttcgtgccc | atctacatct | cctcagagat | cgtcacctta | 360  |
|---|------------|------------|------------|------------|------------|------------|------|
|   | cctgagtaca | ttcagaagcg | ctacgggggc | cagcggatcc | gcatgtacct | gtctgtcctg | 420  |
|   | tccctgctac | tgtctgtctt | caccaagata | tcgctggacc | tgṭacgcggg | ggctctgttt | 480  |
|   | gtgcacatct | gcctgggctg | gaacttctac | ctctccacca | tcctcacgct | cggcatcaca | 540  |
|   | gccctgtaca | ccatcgcagg | gggcctggct | gctgtaatct | acacggacgc | cctgcagacg | 600  |
|   | ctcatcatgg | tggtggggc  | tgtcatcctg | acaatcaaag | cttttgacca | gatcggtggt | 660  |
|   | tacgggcagc | tggaggcagc | ctacgcccag | gccattccct | ccaggaccat | tgccaacacc | 720  |
|   | acctgccacc | tgccacgtac | agacgccatg | cacatgtttc | gagaccccca | cacaggggac | 780  |
|   | ctgccgtgga | ccgggatgac | ctttggcctg | accatcatgg | ccacctggta | ctggtgcacc | 840  |
|   | gaccaggtca | tcgtgcagcg | atcactgtca | gcccgggacc | tgaaccatgc | caaggcgggc | 900  |
|   | tccatcctgg | ccagctacct | caagatgctc | cccatgggcc | tgatcataat | gccgggcatg | 960  |
|   | atcagccgcg | cattgttccc | agatgatgtg | ggctgcgtgg | tgccgtccga | gtgcctgcgg | 1020 |
|   | gcctgcgggg | ccgaggtcgg | ctgctccaac | atcgcctacc | ccaagctggt | catggaactg | 1080 |
|   | atgcccatcg | gtctgcgggg | gctgatgatc | gcagtgatgc | tggcggcgct | catgtcgtcg | 1140 |
|   | ctgacctcca | tcttcaacag | cagcagcacc | ctcttcacta | tggacatctg | gaggcggctg | 1200 |
| ٠ | cgtccccgct | ccggcgagcg | ggagctcctg | ctggtgggac | ggctggtcat | agtggcactc | 1260 |
|   | atcggcgtga | gtgtggcctg | gatccccgtc | ctgcaggact | ccaacagcgg | gcaactcttc | 1320 |
|   | atctacatgc | agtcagtgac | cagctccctg | gccccaccag | tgactgcagt | ctttgtcctg | 1380 |
|   | ggcgtcttct | ggcgacgtgc | caacgagcag | ggggccttct | ggggcctgat | agcagggctg | 1440 |
|   | gtggtgggg  | ccacgaggct | ggtcctggaa | ttcctgaacc | cagccccacc | gtgcggagag | 1500 |
|   | ccagacacgc | ggccagccgt | cctggggagc | atccactacc | tgcacttcgc | tgtcgccctc | 1560 |
|   | tttgcactca | gtggtgctgt | tgtggtggct | ggaagcctgc | tgaccccacc | cccacagagt | 1620 |
|   | gtccagattg | agaaccttac | ctggtggacc | ctggctcagg | atgtgccctt | gggaactaaa | 1680 |
|   | gcaggtgatg | gccaaacacc | ccagaaacac | gccttctggg | cccgtgtctg | tggcttcaat | 1740 |
|   | gccatcctcc | tcatgtgtgt | caacatattc | ttttatgcct | acttcgcctg | a          | 1791 |

300/346

<210> 135

<211> 1404

<212> DNA

5 <213> Homo sapiens

<400> 135

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15

20

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#### 301/346

ggccctgtcc aagccctcat ggaggtgcat gaggacttct tcctatacaa gggaggcatc 1140
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tcagtcaaga tcacaggatg gggagaggag acgctgccag atggaaggac gctcaaatac 1260
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<210> 136

<211> 1431

10 <212> DNA

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15

20

25

<213> Homo sapiens

<400> 136

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5

10

#### 302/346

tgggcagate tgagggetet ggcaagaaat etcatetttg gacteateae etgeetgace 840
ggagteetgg gtgtgggeet gggtgtggag atcageegee ggeteegeea etceaaeeee 900
egggetgate ecctggtetg tgceaetgge etcetggget etgeaeeett ectetteetg 960
tecettgeet gegeeegtgg tageategtg gecaettata tttteatett eattggagag 1020
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cagetgeaeg tgeagggeet getgeaegaa geagggteea eagaegaeeg gattgtggtg 1380
ecceageggg geegeteeae eegegtgeee gtggeeagtg tgeteatetg a 1431

<210> 137

15 <211> 1350

<212> DNA

<213> Homo sapiens

<400> 137

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gacaagggee cegtggaget getggaggag ttegtgttee aggtgeecaa ggagegeage 180

gegeageeca agagaetgaa tteeetteag gagetteaac ttettgaaat catgtgeaat 240

tatteeagg ageaaaceaa ggactetgtt eggeagatta ttttteate cettteage 300

25 ceteaaggga acaaageega tgacageegg atgagettgt tgggaaaact ggteteeatg 360

### 303/346

| gcggtggctg | tgtgtcgaat | cccggtgttg | gagtgtgctg | cctcctggct | tcagcggacg | 420  |
|------------|------------|------------|------------|------------|------------|------|
| cccgtggttt | actgtgtgag | gttagccaag | gcccttgtag | atgactactg | ctgtttggtg | 480  |
| ccgggatcca | ttcagacgct | gaagcagata | ttcagtgcca | gcccgagatt | ctgctgccag | 540  |
| ttcatcacct | ccgttaccgc | gctctatgac | ctgtcatcag | atgacctcat | tccacctatg | 600  |
| gacttgcttg | aaatgattgt | cacctggatt | tttgaggacc | caaggttgat | tctcatcact | 660  |
| tttttaaata | ctccgattgc | ggccaatctg | ccaataggat | tcttagagct | caccccgctc | 720  |
| gttggattga | tccgctggtg | cgtgaaggca | cccctggctt | ataaaaggaa | aaagaagccc | 780  |
| cccttatcca | atggccatgt | cagcaacaag | gtcacaaagg | acccgggcgt | ggggatggac | 840  |
| agagactccc | acctcttgta | ctcaaaactc | cacctcagcg | tcctgcaagt | gctcatgacg | 900  |
| ctgcagctgc | acctgaccga | gaagaatctg | tatgggcgcc | tggggctgat | cctcttcgac | 960  |
| cacatggtcc | cgctggtaga | ggagatcaac | aggttggcgg | atgaactgaa | cccctcaac  | 1020 |
| gcctcccagg | agattgagct | ctcgctggac | cggctggcgc | aggctctgca | ggtggccatg | 1080 |
| gcctcaggag | ctctgctgtg | cacgagagat | gacctgagaa | ccttgtgctc | caggetgeec | 1140 |
| cataataacc | tcctccagct | ggtgatctcg | ggtcccgtgc | agcagtcgcc | tcacgccgcg | 1200 |
| ctcccccgg  | ggttctaccc | ccacatccac | acgcccccgc | tgggctacgg | ggctgtcccg | 1260 |
| gcccaccccg | ccgcccaccc | cgccctgccc | acgcaccccg | gccacacctt | catctccggc | 1320 |
| gtgacctttc | ccttcaggcc | catccgctag |            |            |            | 1350 |

<210> 138

20 <211> 318

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15

<212> DNA

<213> Homo sapiens

<400> 138

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### 304/346

|    | ctaatagcct | tggagatcat | ggttggtggt | cactctcttt | gcttcaactt | cactataaaa | 120 |
|----|------------|------------|------------|------------|------------|------------|-----|
|    | tcattgtcca | gacctggaca | gccctggtgt | gaagcgcagg | tcttcttgaa | taaaaatctt | 180 |
|    | ttccttcagt | acaacagtga | caacaacatg | gtcaaacctc | tgggcctcct | ggggaagaag | 240 |
|    | gtaaatgcca | ccagcacttg | gggagaaaac | ccaaacgctg | ggagaagtgg | ggcgagacct | 300 |
| 5  | caggatgete | ctttgtga   |            |            |            |            | 318 |
|    |            |            |            |            |            |            |     |
|    | <210> 139  |            |            |            |            |            |     |
|    | <211> 246  |            |            |            |            |            |     |
|    | <212> DNA  |            |            |            |            |            |     |
| 10 | <213> Homo | sapiens    |            |            |            |            |     |
|    |            |            |            | •          |            |            |     |
|    | <400> 139  |            |            |            |            |            |     |
|    | atgagccctg | atgtgcgctt | tctgctcctg | ctcctgctcc | tgccccttcg | gaggcctgtg | 60  |
|    | ccagtggcag | ctgggcccgg | agacaccagg | ccggcactgc | tctctttcga | ggcacccgtg | 120 |
| 15 | tttgtgccga | cgctgactcc | cggttgtctg | cagcagccac | gtggccgaaa | tggagcctct | 180 |
|    | ccacgggggc | tccttcccca | gcccctggat | ggcacagcag | cctctcctgt | ctgtcaccac | 240 |
|    | gtgtga     |            |            |            |            |            | 246 |
|    |            |            |            |            |            |            |     |
|    | <210> 140  |            |            |            |            |            |     |
| 20 | <211> 1659 |            |            |            |            |            |     |
|    | <212> DNA  |            |            |            |            |            |     |

<400> 140

<213> Homo sapiens

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5

10

15

20

25

#### 305/346

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Gln Arg Trp Lys Ile Pro Ser Phe Lys Glu Asn Gln Thr Leu Ser Met

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|----|---------|-------|-----|-----|-----|-----|-----|------------------|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Val Met | Tyr   | Ile | Pro | Gln | Thr | Phe | Thr              | Gln | Thr | Ser | Glu | Thr | Ala | Met |     |
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| 5  | Val Glr | Val   | Gln | Glu | Leu | Phe | Pro | Pro              | Pro | Val | Leu | Ser | Ala | Ile | Pro |     |
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|    | Ser Pro | Glu   | Pro | Arg | Glu | Gly | Ser | Leu              | Val | Thr | Leu | Arg | Cys | Gln | Thr |     |
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|    | Lys Leu | His   | Pro | Leu | Arg | Ser | Ala | Leu              | Arg | Leu | Leu | Phe | Ser | Phe | His |     |
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|    | Lys Asp | Gly   | His | Thr | Leu | Gln | Asp | Arg              | Gly | Pro | His | Pro | Glu | Leu | Cys |     |
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|    | Ile Pro | Gly   | Ala | Lys | Glu | Gly | Asp | Ser              | Gly | Leu | Tyr | Trp | Cys | Glu | Val |     |
|    |         | 130   |     |     |     |     | 135 |                  |     |     |     | 140 |     |     |     |     |
|    | gcc cct | gag   | ggt | ggc | cag | gtc | cag | aag <sup>.</sup> | cag | agc | ccc | cag | ctg | gag | gtc | 661 |
| 20 | Ala Pro | Glu   | Gly | Gly | Gln | Val | Gln | Lys              | Gln | Ser | Pro | Gln | Leu | Glu | Val |     |
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|    | Arg Val | Gln . | Ala | Pro | Val | Ser | Arg | Pro              | Val | Leu | Thr | Leu | His | His | Gly |     |
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| 25 | cct gct | gac   | cct | gct | gtg | ggg | gac | atgʻ             | ata | caq | ctc | ctc | tat | σασ | αca | 757 |

|      | Pr | 0 ] | Ala | Asp | Pro | Ala | Val | Gly | Asp | Met | Val | Gln | Leu | Leu | Cys | Glu | Ala |      |
|------|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
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|      | Ca | g a | agg | ggc | tcc | cct | ccg | atc | ctg | tat | tcc | ttc | tac | ctt | gat | gag | aag | 805  |
|      | G1 | n A | Arg | Gly | Ser | Pro | Pro | Ile | Leu | Tyr | Ser | Phe | Tyr | Leu | Asp | Glu | Lys |      |
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|      | Il | e V | /al | Gly | Asn | His | Ser | Ala | Pro | Cys | Gly | Gly | Thr | Thr | Ser | Leu | Leu |      |
|      |    |     |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |      |
|      | tt | CC  | ca  | gtg | aag | tca | gaa | cag | gat | gct | ggg | aac | tac | tcc | tgc | gag | gct | 901  |
| 10   | Ph | e E | Pro | Val | Lys | Ser | Glu | Gln | Asp | Ala | Gly | Asn | Tyr | Ser | Cys | Glu | Ala |      |
|      |    | 2   | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     |      |
|      | ga | g a | ac  | agt | gtc | tcc | aga | gag | agg | agt | gag | ccc | aag | aag | ctg | tct | ctg | 949  |
|      | Gl | u A | lsn | Ser | Val | Ser | Arg | Glu | Arg | Ser | Glu | Pro | Lys | Lys | Leu | Ser | Leu |      |
|      | 24 | 0   |     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |      |
| 15   | aa | g g | ıgt | tct | caa | gtc | ttg | ttc | act | ccc | gcc | agc | aac | tgg | ctg | gtt | cct | 997  |
|      | Ly | s G | ly  | Ser | Gln | Val | Leu | Phe | Thr | Pro | Ala | Ser | Asn | Trp | Leu | Val | Pro |      |
|      |    |     | •   |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |      |
|      | tg | gc  | tt  | cct | gcg | agc | ctg | ctt | ggc | ctg | atg | gtt | att | gct | gct | gca | ctt | 1045 |
|      | Tr | ρL  | eu  | Pro | Ala | Ser | Leu | Leu | Gly | Leu | Met | Val | Ile | Ala | Ala | Ala | Leu |      |
| · 20 |    |     | ,   |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |      |
|      | ct | g g | tt  | tat | gtg | aga | tcc | tgg | aga | aaa | gct | ggg | ccc | ctt | cca | tcc | cag | 1093 |
|      | Le | ı V | al  | Tyr | Val | Arg | Ser | Trp | Arg | Lys | Ala | Gly | Pro | Leu | Pro | Ser | Gln |      |
|      |    |     |     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |      |
|      | at | a c | ca  | ccc | aca | gct | cca | ggt | gga | gag | cag | tgc | cca | cta | tat | gcc | aac | 1141 |
| 25   | 11 | e P | ro  | Pro | Thr | Ala | Pro | Gly | Gly | Glu | Gln | Cys | Pro | Leu | Tyr | Ala | Asn |      |

|    |      | 305   |       |       |       |       | 310   |       |       |       |      | 315  |       |       |       |        |      |
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|    | gtg  | cat   | cac   | cag   | aaa   | ggg   | aaa   | gat   | gaa   | ggt   | gtt  | gtc  | tac   | tct   | gtg   | gtg    | 1189 |
|    | Val  | His   | His   | Gln   | Lys   | Gly   | Lys   | Asp   | Glu   | Gly   | Val  | Val  | Tyr   | Ser   | Val   | Val    |      |
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|    | His  | Arg   | Thr   | Ser   | Lys   | Arg   | Ser   | Glu   | Ala   | Arg   | Ser  | Ala  | Glu   | Phe   | Thr   | Val    |      |
| ,  |      |       |       |       | 340   |       |       |       |       | 345   |      |      |       |       | 350   |        |      |
|    | ggg  | aga   | aag   | gac   | agt   | tct   | atc   | atc   | tgt   | gcg   | gag  | gtg  | aga   | tgc   | ctg   | cag    | 1285 |
|    | Gly  | Arg   | Lуs   | Asp   | Ser   | Ser   | Ile   | Ile   | Cys   | Ala   | Glu  | Val  | Arg   | Суз   | Leu   | Gln    |      |
| 10 |      |       |       | 355   |       |       |       |       | 360   |       |      |      |       | 365   |       |        |      |
|    | ccc  | agt   | gag   | gtt   | tca   | tcc   | acg   | gag   | gtg   | aat   | atg  | aga  | agc   | agg   | act   | ctc    | 1333 |
|    | Pro  | Ser   | Glu   | Val   | Ser   | Ser   | Thr   | Glu   | Val   | Asn   | Met  | Arg  | Ser   | Arg   | Thr   | Leu    |      |
|    |      |       | 370   |       |       |       |       | 375   |       |       |      |      | 380   |       |       |        |      |
|    | caa  | gaa   | ccc   | ctt   | agc   | gac   | tgt   | gag   | gag   | gtt   | ctc  | tgc  | tag   | tgai  | tggtg | jtt    | 1382 |
| 15 | Gln  | Glu   | Pro   | Leu   | Ser   | Asp   | Cys   | Glu   | Glu   | Val   | Leu  | Cys  |       |       |       |        |      |
|    |      | 385   |       |       |       |       | 390   |       |       |       |      | 395  |       |       |       |        |      |
|    | ctc  | ctato | caa d | cacao | egced | ca co | ccca  | agtct | : cca | gtgo  | ctcc | tcag | ggaag | gac a | agtgg | ggtcc  | 1442 |
|    | tcaa | actc  | ttt d | ctgt  | ggto  | c tt  | cagt  | ctcc  | c aag | jccca | agca | tcad | cagag | gcc ( | cct   | gagece | 1502 |
|    | ttgi | cct   | ggt d | cagga | agcad | c to  | gaaco | cctg  | gtt   | cttt  | tct  | tago | cagaa | aga d | ccaac | caatg  | 1562 |
| 20 | gaat | ggga  | aag g | ggaga | atgct | :c c  | cacca | acac  | c aca | cact  | tag  | gtto | caato | cag t | tgaca | ectgga | 1622 |
|    | caca | taaq  | gcc a | acaga | atgto | et to | ettte | cata  | a caa | igcat | gtt  | agtt | cgc   | ccc a | aatat | acata  | 1682 |
|    | tata | atato | gaa a | atagt | cato  | gt go | cgca  | ataad | aac   | attt  | cag  | tcag | gtgat | ag a  | actgo | cataca | 1742 |
|    | caad | cagto | ggt d | ccat  | aaga  | ac to | gtaat | ggag  | ; ttt | aaaa  | aatt | ccta | actgo | cct a | agtga | atatca | 1802 |
|    | tagi | tgc   | ctt a | acat  | cata  | aa ca | acaad | cacat | tto   | ctcac | cgcg | tttç | gtggt | ga 1  | tgcto | gtaca  | 1862 |
| 25 | aaca | aagct | tac a | agcgo | ccgct | a gt  | cata  | ataca | ı aat | atac  | gcac | atao | caatt | at o  | gtaca | agtaca | 1922 |

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| 15 | Met Ala Phe Ser Lys Leu Leu Glu Gln Ala Gly Gly Va  | L Gly Leu Phe |      |
|    | 1 5 10  | 15            |      |
|    | cag acc ctg cag gtg ctc acc ttc atc ctc ccc tgc ctc | c atg ata cct | 153  |
|    | Gln Thr Leu Gln Val Leu Thr Phe Ile Leu Pro Cys Le  | u Met Ile Pro |      |
|    | 20 25   | 30            |      |
| 20 | tcc cag atg ctc ctg gag aac ttc tca gcc gcc atc cc  | a ggc cac cga | 201  |
|    | Ser Gln Met Leu Leu Glu Asn Phe Ser Ala Ala Ile Pr  | o Gly His Arg |      |
|    | 35 40 4   | 5             |      |
|    | tgc tgg aca cac atg ctg gac aat ggc tct gcg gtt tc  | c aca aac atg | 249  |
|    | Cys Trp Thr His Met Leu Asp Asn Gly Ser Ala Val Se  | r Thr Asn Met |      |
| 25 | 50 55 60  |               |      |

|    | acc | CCC | aag | gcc | ctt | ctg | acc  | atc | tcc              | atc | ccg | cca | ggc  | CCC | aac | cag | 297 |
|----|-----|-----|-----|-----|-----|-----|------|-----|------------------|-----|-----|-----|------|-----|-----|-----|-----|
|    | Thr | Pro | Lys | Ala | Leu | Leu | Thr  | Ile | Ser              | Ile | Pro | Pro | Gly  | Pro | Așn | Gln |     |
|    | 65  |     |     |     |     | 70  |      |     |                  |     | 75  |     |      |     |     | 80  |     |
|    | ggg | ccc | cac | cag | tgc | cgc | cgc  | ttc | cgc              | cag | cca | cag | tgg  | cag | ctc | ttg | 345 |
| 5  | Gly | Pro | His | Gln | Cys | Arg | Arg  | Phe | Arg              | Gln | Pro | Gln | Trp  | Gln | Leu | Leu |     |
|    |     |     |     |     | 85  |     |      |     |                  | 90  |     |     |      |     | 95  |     |     |
|    | gac | ccc | aat | gcc | acg | gcc | acc  | agc | tgg              | agc | gaa | gct | gac  | acg | gag | ccg | 393 |
|    | Asp | Pro | Asn | Ala | Thr | Ala | Thr. | Ser | Trp              | Ser | Glu | Ala | Asp  | Thr | Glu | Pro |     |
|    |     |     |     | 100 |     |     |      |     | 105              |     |     |     |      | 110 |     |     |     |
| 10 | tgt | gtg | gac | ggc | tgg | gtc | tat  | gac | cgc              | agc | gtc | ttc | acc  | tcc | acc | atc | 441 |
|    | Cys | Val | Asp | Gly | Trp | Val | Tyr  | Asp | Arg              | Ser | Val | Phe | Thr  | Ser | Thr | Ile |     |
|    |     |     | 115 |     |     |     |      | 120 |                  |     |     |     | 125° |     |     |     |     |
|    | gtg | gcc | aag | tgg | gac | ctg | gtg  | tgc | agc              | tcc | cag | ggc | ttg  | aag | ccc | cta | 489 |
|    | Val | Ala | Lys | Trp | Asp | Leu | Val  | Cys | Ser              | Ser | Gln | Gly | Leu  | Lys | Pro | Leu |     |
| 15 |     | 130 |     |     |     |     | 135  |     |                  |     |     | 140 |      |     |     |     |     |
|    | agc | cag | tcc | atc | ttc | atg | tcc  | ggg | atc              | ctg | gtg | ggc | tcc  | ttt | atc | tgg | 537 |
|    | Ser | Gln | Ser | Ile | Phe | Met | Ser  | Gly | Ile              | Leu | Val | Gly | Ser  | Phe | Ile | Trp |     |
|    | 145 |     |     |     |     | 150 |      |     |                  |     | 155 |     |      |     |     | 160 |     |
|    | ggc | ctc | ctc | tcc | tac | cgg | ttt  | ggg | agg <sub>.</sub> | aag | ccg | atg | ctg  | agc | tgg | tgc | 585 |
| 20 | Gly | Leu | Leu | Ser | Tyr | Arg | Phe  | Gly | Arg              | Lys | Pro | Met | Leu  | Ser | Trp | Cys |     |
|    |     |     |     |     | 165 |     |      |     |                  | 170 |     |     |      |     | 175 |     |     |
|    | tgc | ctg | cag | ttg | gcc | gtg | gcg  | ggc | acc              | agc | acc | atc | ttc  | gcc | cca | aca | 633 |
|    | Суз | Leu | Gln | Leu | Ala | Val | Ala  | Gly | Thr              | Ser | Thr | Ile | Phe  | Ala | Pro | Thr |     |
|    |     |     |     | 180 |     |     |      |     | 185              |     |     |     |      | 190 |     |     |     |
| 25 | ttc | gtc | atc | tac | tgc | ggc | ctg  | cgg | ttc              | gtg | gcc | gct | ttt  | ggg | atg | gcc | 681 |

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|    | Phe | Val | Ile | Tyr | Cys | Gly | Leu | Arg | Phe | Val | Ala | Ala | Phe | Gly | Met | Ala |      |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|    |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |      |
|    | ggc | atc | ttt | ctg | agt | tca | ctg | aca | ctg | atg | gtg | gag | tgg | acc | acg | acc | 729  |
|    | Gly | Ile | Phe | Leu | Ser | Ser | Leu | Thr | Leu | Met | Val | Glu | Trp | Thr | Thr | Thr |      |
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|    | agc | agg | agg | gcg | gtc | acc | atg | acg | gtg | gtg | gga | tgt | gcc | ttc | agc | gca | 777  |
|    | Ser | Arg | Arg | Ala | Val | Thr | Met | Thr | Val | Val | Gly | Cys | Ala | Phe | Ser | Ala |      |
|    | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |      |
|    | ggc | cag | gcg | gcg | ctg | ggc | ggc | ctg | gcc | ttt | gcc | ctg | cgg | gac | tgg | agg | 825  |
| 10 | Gly | Gln | Ala | Ala | Leu | Gly | Gly | Leu | Ala | Phe | Ala | Leu | Arg | Asp | Trp | Arg |      |
|    |     |     |     |     | 245 |     | •   |     |     | 250 |     |     |     |     | 255 |     |      |
|    | act | ctc | cag | ctg | gca | gca | tca | gtg | CCC | ttc | ttt | gcc | atc | tcc | ctg | ata | 873  |
|    | Thr | Leu | Gln | Leu | Ala | Ala | Ser | Val | Pro | Phe | Phe | Ala | Ile | Ser | Leu | Ile |      |
|    |     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |      |
| 15 | tcc | tgg | tgg | ctg | cca | gaa | tcc | gcc | cgg | tgg | ctg | att | att | aag | ggc | aaa | 921  |
|    | Ser | Trp | Trp | Leu | Pro | Glu | Ser | Ala | Arg | Trp | Leu | Ile | Ile | Ъуs | Gly | Lys |      |
|    |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |      |
|    | cca | gac | caa | gca | ctt | cag | gag | ctc | aga | aag | gtg | gcc | agg | ata | aat | ggc | 969  |
|    | Pro | Asp | Gln | Ala | Leu | Gln | Glu | Leu | Arg | Lys | Val | Ala | Arg | Ile | Asņ | Gly |      |
| 20 |     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |      |
|    | cac | aag | gag | gcc | aag | aac | ctg | acc | ata | gag | gtg | ctg | atg | tcc | agc | gtg | 1017 |
|    | His | Lys | Glu | Ala | Lys | Asn | Leu | Thr | Ile | Glu | Val | Leu | Met | Ser | Ser | Val |      |
|    | 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |      |
|    | aag | gag | gag | gtg | gcc | tct | gca | aag | gag | ccg | cgg | tcg | gtg | ctg | gac | ctg | 1065 |
| 25 | Lys | Glu | Glu | Val | Ala | Ser | Ala | Lys | Glu | Pro | Ara | Ser | Val | Leu | Asp | Leu |      |

|      |                   |                          |                                 |                          | 325                             |                          |                   |                                 |                          | 330                      |                   |                   |                          |                   | 335                      |                   |      |
|------|-------------------|--------------------------|---------------------------------|--------------------------|---------------------------------|--------------------------|-------------------|---------------------------------|--------------------------|--------------------------|-------------------|-------------------|--------------------------|-------------------|--------------------------|-------------------|------|
|      | ttc               | tgc                      | gtg                             | ccc                      | gtg                             | ctc                      | cgc               | tgg                             | agg                      | agc                      | tgc               | gcc               | atg                      | ctg               | gtg                      | gtg               | 1113 |
|      | Phe               | Cys                      | Val                             | Pro                      | Val                             | Leu                      | Arg               | Trp                             | Arg                      | Ser                      | Cys               | Ala               | Met                      | Leu               | Val                      | Val               |      |
|      |                   |                          |                                 | 340                      |                                 |                          |                   |                                 | 345                      |                          |                   |                   |                          | 350               |                          |                   |      |
| 5    | aat               | ttc                      | tct                             | cta                      | ttg                             | atc                      | tcc               | tac                             | tat                      | ggg                      | ctg               | gtc               | ttc                      | gac               | ctg                      | cag               | 1161 |
|      | Asn               | Phe                      | Ser                             | Leu                      | Leu                             | Ile                      | Ser               | Tyr                             | Tyr                      | Gly                      | Leu               | Val               | Phe                      | Asp               | Leu                      | Gln               |      |
|      |                   | •                        | 355                             |                          |                                 |                          |                   | 360                             |                          |                          |                   |                   | 365                      |                   |                          |                   |      |
|      | agc               | ctg                      | ggc                             | cgt                      | gac                             | atc                      | ttc               | ctc                             | ctc                      | cag                      | gcc               | ctc               | ttc                      | ggg               | gcc                      | gtg               | 1209 |
|      | Ser               | Leu                      | Gly                             | Arg                      | Asp                             | Ile                      | Phe               | Leu                             | Leu                      | Gln                      | Ala               | Leu               | Phe                      | Gly               | Ala                      | Val               |      |
| 10   |                   | 370                      |                                 |                          | •                               |                          | 375               |                                 |                          |                          |                   | 380               |                          |                   |                          |                   |      |
|      | gac               | ttc                      | ctg                             | ggc                      | cgg                             | gcc                      | acc               | act                             | gcc                      | ctc                      | ttg               | ctc               | agt                      | ttc               | ctt                      | ggc               | 1257 |
|      | Asp               | Phe                      | Leu                             | Gly                      | Arg                             | Ala                      | Thr               | Thr                             | Ala                      | Leu                      | Leu               | Leu               | Ser                      | Phe               | Leu                      | Gly               |      |
|      | 385               |                          |                                 |                          |                                 | 390                      |                   |                                 |                          |                          | 395               |                   |                          |                   |                          | 400               |      |
|      | cgc               | cgc                      | acc                             | atc                      | cag                             | gcg                      | ggt               | tec                             | cag                      | gcc                      | atg               | gcc               | ggc                      | ctc               | gcc                      | att               | 1305 |
| 15   | Arg               | Arg                      | Thr                             | Ile                      | Gln                             | Ala                      | Gly               | Ser                             | Gln                      | Ala                      | Met               | Ala               | Gly                      | Leu               | Ala                      | Ile               | •    |
|      |                   |                          |                                 |                          | 405                             |                          |                   |                                 |                          |                          |                   |                   |                          |                   |                          |                   |      |
|      |                   |                          |                                 |                          | 405                             |                          |                   |                                 |                          | 410                      |                   |                   |                          |                   | 415                      |                   |      |
|      | cta               | gcc                      | aac                             | atg                      |                                 | gtg                      | ccg               | caa                             | gat                      |                          | cag               | acc               | ctg                      | cgt               |                          | gtc               | 1353 |
|      |                   |                          |                                 |                          | ctg                             |                          |                   |                                 |                          | ttg                      |                   |                   | -                        | cgt<br>Arg        | gtg                      |                   | 1353 |
|      |                   |                          |                                 |                          | ctg                             |                          |                   |                                 |                          | ttg                      |                   |                   | -                        | -                 | gtg                      |                   | 1353 |
| . 20 |                   | Ala                      | Asn                             | Met<br>420               | ctg<br>Leu                      | Val                      | Pro               | Gln                             | Asp<br>425               | ttg<br>Leu               | Gln               | Thr               | Leu                      | Arg               | gtg<br>Val               | Val               | 1353 |
| 20   | Leu               | Ala<br>gct               | Asn<br>gtg                      | Met<br>420<br>ctg        | ctg<br>Leu<br>gga               | Val<br>aag               | Pro<br>gga        | Gln<br>tgt                      | Asp<br>425<br>ttt        | ttg<br>Leu<br>ggg        | Gln               | Thr               | Leu<br>cta               | Arg               | gtg<br>Val<br>tgc        | Val<br>ctc        |      |
| 20   | Leu               | Ala<br>gct               | Asn<br>gtg                      | Met<br>420<br>ctg        | ctg<br>Leu<br>gga               | Val<br>aag               | Pro<br>gga        | Gln<br>tgt                      | Asp<br>425<br>ttt        | ttg<br>Leu<br>ggg        | Gln               | Thr               | Leu<br>cta               | Arg<br>430<br>acc | gtg<br>Val<br>tgc        | Val<br>ctc        |      |
| 20   | Leu<br>ttt<br>Phe | Ala<br>gct<br>Ala        | Asn<br>gtg<br>Val<br>435        | Met<br>420<br>ctg<br>Leu | ctg<br>Leu<br>gga<br>Gly        | Val<br>aag<br>Lys        | Pro<br>gga<br>Gly | Gln<br>tgt<br>Cys<br>440        | Asp<br>425<br>ttt<br>Phe | ttg<br>Leu<br>ggg<br>Gly | Gln<br>ata<br>Ile | Thr<br>agc<br>Ser | Leu<br>cta<br>Leu<br>445 | Arg<br>430<br>acc | gtg<br>Val<br>tgc<br>Cys | Val<br>ctc<br>Leu |      |
| 20   | Leu<br>ttt<br>Phe | Ala<br>gct<br>Ala<br>atc | Asn<br>gtg<br>Val<br>435<br>tac | Met<br>420<br>ctg<br>Leu | ctg<br>Leu<br>gga<br>Gly<br>gct | Val<br>aag<br>Lys<br>gaa | Pro<br>gga<br>Gly | Gln<br>tgt<br>Cys<br>440<br>ttt | Asp<br>425<br>ttt<br>Phe | ttg<br>Leu<br>ggg<br>Gly | Gln<br>ata<br>Ile | Thr<br>agc<br>Ser | Leu<br>cta<br>Leu<br>445 | Arg 430 acc Thr   | gtg<br>Val<br>tgc<br>Cys | Val<br>ctc<br>Leu | 1401 |

|    | gat  | ggc   | att   | ctg   | cat   | aca   | gtg  | ggc   | cgg   | ctg   | ggg  | gct  | atg   | atg   | ggt   | ccc   | 1497 |
|----|------|-------|-------|-------|-------|-------|------|-------|-------|-------|------|------|-------|-------|-------|-------|------|
|    | Asp  | Gly   | Ile   | Leu   | His   | Thr   | Val  | Gly   | Arg   | Leu   | Gly  | Ala  | Met   | Met   | Gly   | Pro   | •    |
|    | 465  |       |       |       |       | 470   |      |       |       | •     | 475  |      |       |       |       | 480   |      |
|    | ctg  | atc   | ctg   | atg   | agc   | cgc   | caa  | gcc   | ctg   | ccc   | ctg  | ctg  | cct   | cct   | ctc   | ctc   | 1545 |
| 5  | Leu  | Ile   | Leu   | Met   | Ser   | Arg   | Gln  | Ala   | Leu   | Pro   | Leu  | Leu  | Pro   | Pro   | Leu   | Leu   |      |
|    |      |       |       |       | 485   |       |      |       |       | 490   |      |      |       |       | 495   |       |      |
|    | tat  | ggc   | gtt   | atc   | tcc   | att   | gct  | tcc   | agc   | ctg   | gtt  | gtg  | ctg   | ttc   | ttc   | ctc   | 1593 |
|    | Tyr  | Gly   | Val   | Ile   | Ser   | Ile   | Ala  | Ser   | Ser   | Leu   | Val  | Val  | Leu   | Phe   | Phe   | Leu   |      |
|    |      |       |       | 500   |       |       |      |       | 505   |       |      |      |       | 510   |       |       |      |
| 10 | ccg  | gag   | acc   | cag   | gga   | ctt   | ccg  | ctc   | cct   | gac   | act  | atc  | cag   | gac   | ctg   | gag   | 1641 |
|    | Pro  | Glu   | Thr   | Gln   | Gly   | Leu   | Pro  | Leu   | Pro   | Asp   | Thr  | Ile  | Gln   | Asp   | Leu   | Glu   |      |
|    |      |       | 515   |       |       |       |      | 520   |       |       |      |      | 525   |       |       |       |      |
|    | agc  | cag   | aaa   | tca   | aca   | gca   | gcc  | cag   | ggc   | aac   | cgg  | caa  | gag   | gcc   | gtc   | act   | 1689 |
|    | Ser  | Gln   | Lys   | Ser   | Thr   | Ala   | Ala  | Gln   | Gly   | Asn   | Arg  | Gln  | Glu   | Ala   | Val   | Thr   |      |
| 15 |      | 530   |       |       |       |       | 535  |       |       |       |      | 540  |       |       |       |       |      |
|    | gtg  | gaà   | agt   | acc   | tcg   | ctc   | tag  | aaat  | tgtç  | gcc t | gcat | ggag | jc co | cttt  | cagto | :     | 1740 |
|    | Val  | Glu   | Ser   | Thr   | Ser   | Leu   |      |       |       |       |      |      |       |       |       |       |      |
|    | 545  |       |       |       |       | 550   |      |       |       |       |      |      |       |       |       |       |      |
|    | aaag | acto  | cct o | ggaaa | ıggaç | ıt to | ccto | ettet | . cca | atca  | ıgag | cgto | gagg  | geg a | agtto | ggcga | 1800 |
| 20 | cttc | aagg  | igc d | etggo | atgo  | ıc aç | aggo | cago  | cag   | ccgt  | ggc  | cgaç | gtgga | ıca ç | gcgtg | gccgt | 1860 |
|    | ctgo | etgtg | ggc t | gaag  | gcag  | jc tt | cca  | cagct | cac   | tcct  | ctt  | ctc  | ctgo  | ccc t | gato  | agatt | 1920 |
|    | cccc | acct  | ta d  | ccgg  | gccc  | t ac  | agga | gcct  | gto   | caga  | itgg | ccat | gccc  | caa c | caat  | aacga | 1980 |
|    | gacg | gtto  | cc c  | ctccc | tttc  | c ct  | gcca | iggct | : cat | gtct  | tta  | caco | ettca | act o | cagco | acgcc | 2040 |
|    | aacc | agag  | jac t | gggt  | teca  | a to  | tcac | ccca  | cca   | cata  | cag  | agco | ectca | atc t | gtga  | aatga | 2100 |
| 25 | gaat | gato  | ac g  | gtgac | ccac  | :c cc | ccag | iggca | ggt   | atca  | ıggg | tgaa | ectga | itc t | tago  | accgg | 2160 |

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15 Met Lys His

1

aca ctg gct ctg gct ccc ctg ctg ggc ctg ggc ctg ggc ctg gcc 165
Thr Leu Ala Leu Leu Ala Pro Leu Leu Gly Leu Gly Leu Gly Leu Ala

5 10 15

20 ctg agt cag ctg gct gca ggg gcc aca gac tgc aag ttc ctt ggc ccg 213

Leu Ser Gln Leu Ala Ala Gly Ala Thr Asp Cys Lys Phe Leu Gly Pro

20 25 30 35

gca gag cac ctg aca ttc acc cca gca gcc agg gcc cgg tgg ctg gcc 261
Ala Glu His Leu Thr Phe Thr Pro Ala Ala Arg Ala Arg Trp Leu Ala

25 40 45 50

|    | CCT | cga | gtt | cgt | gcg | cca | gga | CTC | ctg | gac | tcc | CTC | tat | ggc | acc | gtg | 305 |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Pro | Arg | Val | Arg | Ala | Pro | Gly | Leu | Leu | Asp | Ser | Leu | Tyr | Gly | Thr | Val |     |
|    |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     | 65  |     |     |     |
|    | cgc | cgc | ttc | ctc | tcg | gtg | gtg | cag | ctc | aat | cct | ttc | cct | tca | gag | ttg | 357 |
| 5  | Arg | Arg | Phe | Leu | Ser | Val | Val | Gln | Leu | Asn | Pro | Phe | Pro | Ser | Glu | Leu |     |
|    |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |     |     |     |     |
|    | gta | aag | gcc | cta | ctg | aat | gag | ctg | gcc | tcc | gtg | aag | gtg | aat | gag | gtg | 405 |
|    | Val | Lys | Ala | Leu | Leu | Asn | Glu | Leu | Ala | Ser | Val | Lys | Val | Asn | Glu | Val |     |
|    |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |     |     |     |     |
| 10 | gtg | cgg | tac | gag | gcg | ggc | tac | gtg | gta | tgc | gct | gtg | atc | gcg | ggc | ctc | 453 |
|    | Val | Arg | Tyr | Glu | Ala | Gly | Tyr | Val | Val | Cys | Ala | Val | Ile | Ala | Gly | Leu |     |
|    | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |     |     | 115 |     |
|    | tac | ctg | ctg | ctg | gtg | ccc | act | gcc | ggg | ctt | tgc | ttc | tgc | tgc | tgc | cgc | 501 |
|    | Tyr | Leu | Leu | Leu | Val | Pro | Thr | Ala | Gly | Leu | Cys | Phe | Cys | Cys | Суз | Arg |     |
| 15 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |     | 130 |     |     |
|    | tgc | cac | cgg | cgc | tgc | ggg | gga | cga | gtg | aag | aca | gag | cac | aag | gcg | ctg | 549 |
|    | Cys | His | Arg | Arg | Cys | Gly | Gly | Arg | Val | Lys | Thr | Glu | His | Lys | Ala | Leu |     |
|    |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     | 145 |     |     |     |
|    | gcc | tgt | gag | cgc | gcg | gcc | ctc | atg | gtc | ttc | ctg | ctg | ctg | acc | acc | ctc | 597 |
| 20 | Ala | Cys | Glu | Arg | Ala | Ala | Leu | Met | Val | Phe | Leu | Leu | Leu | Thr | Thr | Leu |     |
|    |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |     |     |     |     |
|    | ttg | ctg | ctg | att | ggt | gtg | gtc | tgt | gcc | ttt | gtc | acc | aac | cag | cgc | acg | 645 |
|    | Leu | Leu | Leu | Ile | Gly | Val | Val | Cys | Ala | Phe | Val | Thr | Asn | Gln | Arg | Thr |     |
|    |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |     |     |     |     |
| 25 | cat | gaa | caq | atg | ggc | CCC | agc | atc | σaσ | acc | atq | cct | gag | acc | cta | ctc | 693 |

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His Glu Gln Met Gly Pro Ser Ile Glu Ala Met Pro Glu Thr Leu Leu

180 185 190 195

agc ctc tgg ggc ctg gtc tct gat gtc ccc caa gtg agc act gtt acc 741

Ser Leu Trp Gly Leu Val Ser Asp Val Pro Gln Val Ser Thr Val Thr

5 200 205 210

cct cac cct cat gtg ccc ctg tga gcactgggcc cgggcaggac agagccgagt 795
Pro His Pro His Val Pro Leu

215

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15

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25

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5

10

15

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|----|-----|------|-----|------|------|------|------|------|------|------|------|-----|------|------|------|--------|-----|
|    |     |      |     |      |      |      |      |      |      |      |      | Me  | et A | la A | la A | sn Ser |     |
| 5  |     |      |     |      |      |      |      |      |      |      |      |     | 1    |      |      | 5      |     |
|    | acc | agc  | gac | ctc  | cac  | act  | ccc  | ggg  | acg  | cag  | ctg  | agc | gtg  | gct  | gac  | atc    | 104 |
|    | Thr | Ser  | Asp | Leu  | His  | Thr  | Pro  | Gly  | Thr  | Gln  | Leu  | Ser | Val  | Ala  | Asp  | Ile    |     |
|    |     |      |     |      | 10   |      |      |      |      | 15   |      |     |      |      | 20   |        |     |
|    | atc | gtc  | atc | act  | gtg  | tat  | ttt  | gct  | ctg  | aat  | gtg  | gcc | gtg  | ggc  | ata  | tgg    | 152 |
| 10 | Ile | Val  | Ile | Thr  | Val  | Tyr  | Phe  | Ala  | Leu  | Asn  | Val  | Ala | Val  | Gly  | Ile  | Trp    |     |
|    |     |      |     | 25   |      |      |      |      | 30   |      |      |     |      | 35   |      |        |     |
|    | tcc | tct  | tgt | cgg  | gcc  | agt  | agg  | aac  | acg  | gtg  | aat  | ggc | tac  | ttc  | ctg  | gca    | 200 |
|    | Ser | Ser  | Cys | Arg  | Ala  | Ser  | Arg  | Asn  | Thr  | Val  | Asn  | Gly | Tyr  | Phe  | Leu  | Ala    |     |
|    |     |      | 40  |      |      |      |      | 45   |      |      |      |     | 50   |      |      |        |     |
| 15 | ggc | cgg  | gac | atg  | acg  | tgg  | tgg  | ccg  | att  | gga  | gcc  | tcc | ctc  | ttc  | gcc  | agc    | 248 |
|    | Gly | Arg  | Asp | Met  | Thr  | Trp  | Trp  | Pro  | Ile  | Gly  | Ala  | Ser | Leu  | Phe  | Ala  | Ser    |     |
|    |     | 55   |     |      |      |      | 60   |      |      |      |      | 65  |      |      |      |        |     |
|    | agc | gag  | ggc | tct  | ggc  | ctc  | ttc  | att  | gga  | ctg  | gcg  | ggc | tca  | ggc  | gcg  | gca    | 296 |
|    | Ser | Glu  | Gly | Ser  | Gly  | Leu  | Phe  | Ile  | Gly  | Leu  | Ala  | Gly | Ser  | Gly  | Ala  | Ala    |     |
| 20 | 70  |      |     |      |      | 75   |      |      |      |      | 80   |     |      |      |      | 85     |     |
|    | gga | ggt  | ctg | gcc  | gtg  | gca  | ggc  | ttc  | gag  | tgg  | aat  | gcc | acg  | tac  | gtg  | ctg    | 344 |
|    | Gly | Gly  | Leu | Ala  | Val  | Ala  | Gly  | Phe  | Glu  | Trp  | Asn  | Ala | Thr  | Tyr  | Val  | Leu    |     |
|    |     |      |     |      | 90   |      |      |      | _    | 95   |      |     |      |      | 100  |        |     |
|    | ctg | gca  | ctg | gca  | tgg  | gtg  | ttc  | gtg  | ccc  | atc  | tac  | atc | tcc  | tca  | gag  | atc    | 392 |
| 25 | Leu | Ala  | Leu | Ala  | Trp  | Val  | Phe  | Val  | Pro  | Ile  | Tyr  | Ile | Ser  | Ser  | Glu  | Ile    |     |

|    |     |     |     | 105  |     |     |     |     | 110 |     |     |     |     | 115 |     |     |     |
|----|-----|-----|-----|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | gtc | acc | tta | cct  | gag | tac | att | cag | aag | cgc | tac | ggg | ggc | cag | cgg | atc | 440 |
|    | Val | Thr | Leu | Pro  | Glu | Tyr | Ile | Gln | Lys | Arg | Tyr | Gly | Gly | Gln | Arg | Ile |     |
|    |     |     | 120 |      |     |     |     | 125 |     |     |     |     | 130 |     |     |     |     |
| 5  | cgc | atg | tac | ctg  | tct | gtc | ctg | tcc | ctg | cta | ctg | tct | gtc | ttc | acc | aag | 488 |
|    | Arg | Met | Tyr | Leu  | Ser | Val | Leu | Ser | Leu | Leu | Leu | Ser | Val | Phe | Thr | Lys |     |
|    |     | 135 |     |      |     |     | 140 |     |     |     |     | 145 |     |     |     |     |     |
|    | ata | tcg | ctg | gac  | ctg | tac | gcg | ggg | gct | ctg | ttt | gtg | cac | atc | tgc | ctg | 536 |
|    | Ile | Ser | Leu | Asp  | Leu | Tyr | Ala | Gly | Ala | Leu | Phe | Val | His | Ile | Cys | Leu |     |
| 10 | 150 |     |     | -    |     | 155 |     |     |     |     | 160 |     |     |     |     | 165 |     |
|    | ggc | tgg | aac | ttc  | tac | ctc | tcc | acc | atc | ctc | acg | ctc | ggc | atc | aca | gcc | 584 |
|    | Gly | Trp | Asn | Phe  | Tyr | Leu | Ser | Thr | Ile | Leu | Thr | Leu | Gly | Ile | Thr | Ala |     |
|    |     |     |     |      | 170 |     |     |     |     | 175 |     |     |     |     | 180 |     |     |
|    | ctg | tac | acc | atc  | gca | ggg | ggc | ctg | gct | gct | gta | atc | tac | acg | gac | gcc | 632 |
| 15 | Leu | Tyr | Thr | Ile  | Ala | Gly | Gly | Leu | Ala | Ala | Val | Ile | Tyr | Thr | Asp | Ala |     |
|    |     |     |     | 185  |     |     |     |     | 190 |     |     |     |     | 195 |     |     |     |
|    | ctg | cag | acg | ctc  | atc | atg | gtg | gtg | ggg | gct | gtc | atc | ctg | aca | atc | aaa | 680 |
|    | Leu | Gln | Thr | Leu- | Ile | Met | Val | Val | Gly | Ala | Val | Ile | Leu | Thr | Ile | Lys |     |
|    |     |     | 200 |      |     |     |     | 205 |     |     |     |     | 210 |     |     |     |     |
| 20 | gct | ttt | gac | cag  | atc | ggt | ggt | tac | ggg | cag | ctg | gag | gca | gcc | tac | gcc | 728 |
|    | Ala | Phe | Asp | Gln  | Ile | Gly | Gly | Tyr | Gly | Gln | Leu | Glu | Ala | Ala | Tyr | Ala |     |
|    |     | 215 |     |      |     |     | 220 |     |     |     |     | 225 |     |     |     |     |     |
|    | cag | gcc | att | ccc  | tcc | agg | acc | att | gcc | aac | acc | acc | tgc | cac | ctg | cca | 776 |
|    | Gln | Ala | Ile | Pro  | Ser | Arg | Thr | Ile | Ala | Asn | Thr | Thr | Cys | His | Leu | Pro |     |
| 25 | 230 |     |     |      |     | 235 |     |     |     |     | 240 |     |     |     |     | 245 |     |

|    | cgt | aca | gac | gcc | atg | cac | atg | ttt | cga | gac | ccc | cac | aça | ggg | gac | ctg | 824  |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|    | Arg | Thr | Asp | Ala | Met | His | Met | Phe | Arg | Asp | Pro | His | Thr | Gly | Asp | Leu |      |
|    |     |     |     |     | 250 |     |     |     |     | 255 |     |     |     |     | 260 |     |      |
|    | ccg | tgg | acc | ggg | atg | acc | ttt | ggc | ctg | acc | atc | atg | gcc | acc | tgg | tac | 872  |
| 5  | Pro | Trp | Thr | Gly | Met | Thr | Phe | Gly | Leu | Thr | Ile | Met | Ala | Thr | Trp | Tyr |      |
|    |     |     |     | 265 |     |     |     |     | 270 |     |     |     |     | 275 |     |     |      |
|    | tgg | tgc | acc | gac | cag | gtc | atc | gtg | cag | cga | tca | ctg | tca | gcc | cgg | gac | 920  |
|    | Trp | Cys | Thr | Asp | Gln | Val | Ile | Val | Gln | Arg | Ser | Leu | Ser | Ala | Arg | Asp |      |
|    |     |     | 280 |     |     |     |     | 285 |     |     |     |     | 290 |     |     |     |      |
| 10 | ctg | aac | cat | gcc | aag | gcg | ggc | tcc | atc | ctg | gcc | agc | tac | ctc | aag | atg | 968  |
|    | Leu | Asn | His | Ala | Lys | Ala | Gly | Ser | Ile | Leu | Ala | Ser | Tyr | Leu | Lys | Met |      |
|    |     | 295 |     |     |     |     | 300 |     |     |     |     | 305 |     |     |     |     |      |
|    | ctc | ccc | atg | ggc | ctg | atc | ata | atg | ccg | ggc | atg | atc | agc | cgc | gca | ttg | 1016 |
|    | Leu | Pro | Met | Gly | Leu | Ile | Ile | Met | Pro | Gly | Met | Ile | Ser | Arg | Ala | Leu |      |
| 15 | 310 |     |     |     |     | 315 |     |     |     |     | 320 |     |     |     |     | 325 |      |
|    | ttc | cca | gat | gat | gtg | ggc | tgc | gtg | gtg | ccg | tcc | gag | tgc | ctg | cgg | gcc | 1064 |
|    | Phe | Pro | Asp | Asp | Val | Gly | Cys | Val | Val | Pro | Ser | Glu | Cys | Leu | Arg | Ala | ,    |
|    |     |     |     |     | 330 |     |     |     |     | 335 |     |     |     |     | 340 |     |      |
|    | tgc | ggg | gcc | gag | gtc | ggc | tgc | tcc | aac | atc | gcc | tac | ccc | aag | ctg | gtc | 1112 |
| 20 | Cys | Gly | Ala | Glu | Val | Gly | Суз | Ser | Asn | Ile | Ala | Tyr | Pro | Lys | Leu | Val |      |
|    |     |     |     | 345 |     |     |     |     | 350 |     |     |     |     | 355 |     |     |      |
|    | atg | gaa | ctg | atg | ccc | atc | ggt | ctg | cgg | ggg | ctg | atg | atc | gca | gtg | atg | 1160 |
|    | Met | Glu | Leu | Met | Pro | Ile | Gly | Leu | Arg | Gly | Leu | Met | Ile | Ala | Val | Met |      |
|    |     |     | 360 |     |     |     |     | 365 |     |     |     |     | 370 |     |     |     |      |
| 25 | ctg | gcg | gcg | ctc | atg | tcg | tcg | ctg | acc | tcc | atc | ttc | aac | agc | agc | agc | 1208 |

|    | Leu | Ala | Ala | Leu | Met | Ser | Ser    | Leu | Thr | Ser | Ile | Phe | Asn   | Ser | Ser | Ser |      |
|----|-----|-----|-----|-----|-----|-----|--------|-----|-----|-----|-----|-----|-------|-----|-----|-----|------|
|    |     | 375 |     |     |     |     | 380    |     |     |     |     | 385 |       |     |     |     |      |
|    | acc | ctc | ttc | act | atg | gac | atc    | tgg | agg | cgg | ctg | cgt | ccc   | cgc | tcc | ggc | 1256 |
|    | Thr | Leu | Phe | Thr | Met | Asp | Ile    | Trp | Arg | Arg | Leu | Arg | Pro   | Arg | Ser | Gly |      |
| 5  | 390 |     |     |     |     | 395 |        |     |     |     | 400 |     |       |     |     | 405 |      |
|    | gag | cgg | gag | ctc | ctg | ctg | gtg    | gga | cgg | ctg | gtc | ata | gtg   | gca | ctc | atc | 1304 |
|    | Glu | Arg | Glu | Leu | Leu | Leu | Val    | Gly | Arg | Leu | Val | Ile | Val   | Ala | Leu | Ile |      |
|    |     |     |     |     | 410 |     |        |     |     | 415 |     |     |       |     | 420 |     |      |
|    | ggc | gtg | agt | gtg | gcc | tgg | atc    | ccc | gtc | ctg | cag | gac | tcc   | aac | agc | ggg | 1352 |
| 10 | Gly | Val | Ser | Val | Ala | Trp | Ile    | Pro | Val | Leu | Gln | Asp | Ser   | Asn | Ser | Gly |      |
|    |     |     |     | 425 |     |     |        |     | 430 |     |     |     |       | 435 |     |     |      |
|    | caa | ctc | ttc | atc | tac | atg | cag    | tca | gtg | acc | agc | tcc | ctg   | gcc | сса | cca | 1400 |
|    | Gln | Leu | Phe | Ile | Tyr | Met | Gln    | Ser | Val | Thr | Ser | Ser | Leu   | Ala | Pro | Pro |      |
|    |     |     | 440 |     |     |     |        | 445 |     |     |     |     | 450   |     |     |     |      |
| 15 | gtg | act | gca | gtc | ttt | gtc | ctg    | ggc | gtc | ttc | tgg | cga | cgt   | gcc | aac | gag | 1448 |
|    | Val | Thr | Ala | Val | Phe | Val | Leu    | Gly | Val | Phe | Trp | Arg | Arg   | Ala | Asn | Glu |      |
|    |     | 455 | ٠   |     |     |     | 460    | >   |     |     |     | 465 |       |     |     |     |      |
|    | cag | ggg | gcc | ttc | tgg | ggc | ctg    | ata | gca | ggg | ctg | gtg | gtg   | ggg | gcc | acg | 1496 |
|    | Gln | Gly | Ala | Phe | Trp | Gly | Leu    | Ile | Ala | Gly | Leu | Val | Val   | Gly | Ala | Thr |      |
| 20 | 470 |     |     |     |     | 475 |        |     |     |     | 480 |     |       |     |     | 485 |      |
|    | agg | ctg | gtc | ctg | gaa | ttc | ctg    | aac | cca | gcc | cca | ccg | tgc   | gga | gag | cca | 1544 |
|    | Arg | Leu | Val | Leu | Glu | Phe | Leu    | Asn | Pro | Ala | Pro | Pro | Cys   | Gly | Glu | Pro |      |
|    |     |     |     |     | 490 |     |        |     |     | 495 |     |     |       |     | 500 |     |      |
|    | gac | acg | cgg | cca | gcc | gtc | ctg    | ggg | agc | atc | cac | tac | ctg   | cac | ttc | gct | 1592 |
| 25 | Asp | Thr | Ara | Pro | Ala | ٧a٦ | Ĭ.e.ıı | Glv | Ser | Tle | Hie | ጥህታ | T.e.r | His | Phe | Δla |      |

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|    |      |      |      | 505  |      |      |      |       | 510  |       |     |      |      | 515   |       |       |      |  |
|----|------|------|------|------|------|------|------|-------|------|-------|-----|------|------|-------|-------|-------|------|--|
|    | gtc  | gcc  | ctc  | ttt  | gca  | ctc  | agt  | ggt   | gct  | gtt   | gtg | gtg  | gct  | gga   | agc   | ctg   | 1640 |  |
|    | Val  | Ala  | Leu  | Phe  | Ala  | Leu  | Ser  | Gly   | Ala  | Val   | Val | Val  | Ala  | Gly   | Ser   | Leu   |      |  |
|    |      |      | 520  |      |      |      |      | 525   |      |       |     |      | 530  |       |       |       |      |  |
| 5  | ctg  | acc  | cca  | ccc  | cca  | cag  | agt  | gtc   | cag  | att   | gag | aac  | ctt  | acc   | tgg   | tgg   | 1688 |  |
|    | Leu  | Thr  | Pro  | Pro  | Pro  | Gln  | Ser  | Val   | Gln  | Ile   | Glu | Asn  | Leu  | Thr   | Trp   | Trp   |      |  |
|    |      | 535  |      |      |      |      | 540  |       |      |       |     | 545  |      |       |       |       |      |  |
|    | acc  | ctg  | gct  | cag  | gat  | gtg  | ccc  | ttg   | gga  | act   | aaa | gca  | ggt  | gat   | ggc   | caa   | 1736 |  |
|    | Thr  | Leu  | Ala  | Gln  | Asp  | Val  | Pro  | Leu   | Gly  | Thr   | Lys | Ala  | Gly  | Asp   | Gly   | Gln   |      |  |
| 10 | 550  |      |      |      |      | 555  |      |       |      |       | 560 |      |      |       |       | 565   |      |  |
|    | aca  | ccc  | cag  | aaa  | cac  | gcc  | ttc  | tgg   | gcc  | cgt   | gtc | tgt  | ggc  | ttc   | aat   | gcc   | 1784 |  |
|    | Thr  | Pro  | Gln  | Lys  | His  | Ala  | Phe  | Trp   | Ala  | Arg   | Val | Cys  | Gly  | Phe   | Asn   | Ala   |      |  |
|    |      |      |      |      | 570  |      |      |       |      | 575   |     |      |      |       | 580   |       |      |  |
|    | atc  | ctc  | ctc  | atg  | tgt  | gtc  | aac  | ata   | ttc  | ttt   | tat | gcc  | tac  | ttc   | gcc   | tga   | 1832 |  |
| 15 | Ile  | Leu  | Leu  | Met  | Cys  | Val  | Asn  | Ile   | Phe  | Phe   | Tyr | Ala  | Tyr  | Phe   | Ala   |       |      |  |
|    |      |      |      | 585  |      |      |      |       | 590  |       |     |      |      | 595   |       |       |      |  |
|    | cact | gcca | tc c | tgga | caga | a ag | gcag | gago  | tct: | gagt  | cct | cagg | tcca | icc d | cattt | ccctc | 1892 |  |
|    | atgg | ggat | cc c | gaag | cccc | a ag | aggg | gcag  | att  | .cccc | tca | cagc | tgca | .ca ç | gcago | tcggt | 1952 |  |
|    | gccc | aaga | ac t | ggcc | aago | c ag | caaa | ıgcgg | gag  | ccct  | gaa | aaat | tagg | gg g  | ggaaa | tggga | 2012 |  |
| 20 | gaaa | ataa | tg t | gaca | tttc | a aa | aaca | gcac  | caa  | agca  | gtc | agca | ttgg | aa g  | gaaa  | attag | 2072 |  |
|    | attt | ctga | cg g | ac   |      |      |      |       |      |       |     |      |      |       |       |       | 2085 |  |
|    |      |      |      |      |      |      |      |       |      |       |     |      |      |       |       |       |      |  |

<210> 145

<211> 2208

25 <212> DNA

324/346

<213> Homo sapiens

<220>

<221> CDS

5 <222> (100)..(1503)

<400> 145

10

cttgactttg agcgtccggc ggtcgcagag ccaggaggcg gaggcgcgc ggccagcctg 60

ggccccagcc cacaccttca ccagggccca ggagccacc atg tgg cga tgt cca 114

Met Trp Arg Cys Pro

1 5

ctg ggg cta ctg ctg ttg ctg ccg ctg gct ggc cac ttg gct ctg ggt 162
Leu Gly Leu Leu Leu Leu Pro Leu Ala Gly His Leu Ala Leu Gly

10 15 20

gcc cag cag ggt cgt ggg cgc cgg gag cta gca ccg ggt ctg cac ctg 210

Ala Gln Gln Gly Arg Gly Arg Glu Leu Ala Pro Gly Leu His Leu

25 30 35

cgg ggc atc cgg gac gcg gga ggc cgg tac tgc cag gag cag gac ctg 258 Arg Gly Ile Arg Asp Ala Gly Gly Arg Tyr Cys Gln Glu Gln Asp Leu

20 40 45 50

tgc tgc cgc ggc cgt gcc gac gac tgt gcc ctg ccc tac ctg ggc gcc 306 Cys Cys Arg Gly Arg Ala Asp Asp Cys Ala Leu Pro Tyr Leu Gly Ala

55 60 65

atc tgt tac tgt gac ctc ttc tgc aac cgc acg gtc tcc gac tgc tgc 354

25 Ile Cys Tyr Cys Asp Leu Phe Cys Asn Arg Thr Val Ser Asp Cys Cys

|    | 70  |     |     |     |     | 75  |     |     |     |     | 80  |     |     |     |     | 85  |     |    |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|----|
|    | cct | gac | ttc | tgg | gac | ttc | tgc | ctc | ggc | gtg | cca | ccc | cct | ttt | ccc | ccg | 402 |    |
|    | Pro | Asp | Phe | Trp | Asp | Phe | Cys | Leu | Gly | Val | Pro | Pro | Pro | Phe | Pro | Pro |     |    |
|    |     |     |     |     | 90  |     |     |     |     | 95  |     |     |     |     | 100 |     |     |    |
| 5  | atc | caa | gga | tgt | atg | cat | gga | ggt | cgt | atc | tat | cca | gtc | ttg | gga | acg | 450 |    |
|    | Ile | Gln | Gly | Cys | Met | His | Gly | Gly | Arg | Ile | Tyr | Pro | Val | Leu | Gly | Thr |     |    |
|    |     |     |     | 105 |     |     |     |     | 110 |     |     |     |     | 115 |     |     |     |    |
|    | tac | tgg | gac | aac | tgt | aac | cgt | tgc | acc | tgc | cag | gag | aac | agg | cag | tgg | 498 |    |
|    | Tyr | Trp | Asp | Asn | Суѕ | Asn | Arg | Cys | Thr | Суѕ | Gln | Glu | Asn | Arg | Gln | Trp |     |    |
| 10 |     | -   | 120 |     |     |     |     | 125 |     |     |     |     | 130 |     |     |     |     | Œ  |
|    | cag | tgt | gac | caa | gaa | cca | tgc | ctg | gtg | gat | cca | gac | atg | atc | aaa | gcc | 546 | \$ |
|    | Gln | Cys | Asp | Gln | Glu | Pro | Cys | Leu | Val | Asp | Pro | Asp | Met | Ile | Lys | Ala |     |    |
|    |     | 135 |     |     |     |     | 140 |     |     |     |     | 145 |     |     |     |     |     |    |
|    | atc | aac | cag | ggc | aac | tat | ggc | tgg | cag | gct | ggg | aac | cac | agc | gcc | ttc | 594 |    |
| 15 | Ile | Asn | Gln | Gly | Asn | Tyr | Gly | Trp | Gln | Ala | Gly | Asn | His | Ser | Ala | Phe |     |    |
|    | 150 |     |     |     |     | 155 |     |     |     |     | 160 |     |     |     |     | 165 |     |    |
|    | tgg | ggc | atg | acc | ctg | gat | gag | ggc | att | cgc | tac | cgc | ctg | ggc | acc | atc | 642 |    |
|    | Trp | Gly | Met | Thr | Leu | Asp | Glu | Gly | Ile | Arg | Tyr | Arg | Leu | Gly | Thr | Ile |     |    |
|    |     |     |     |     | 170 |     |     |     |     | 175 |     |     |     |     | 180 |     |     |    |
| 20 | cgc | cca | tct | tcc | tcg | gtc | atg | aac | atg | cat | gaa | att | tat | aca | gtg | ctg | 690 |    |
|    | Arg | Pro | Ser | Ser | Ser | Val | Met | Asn | Met | His | Glu | Ile | Tyr | Thr | Val | Leu |     |    |
|    |     |     |     | 185 |     |     |     |     | 190 |     |     |     |     | 195 |     |     |     |    |
|    |     |     |     | gag |     |     |     |     |     |     |     |     |     |     |     | _   | 738 |    |
|    | Asn | Pro | Gly | Glu | Val | Leu | Pro | Thr | Ala | Phe | Glu | Ala | Ser | Glu | Lys | Trp |     |    |
| 25 |     |     | 200 |     |     |     |     | 205 |     |     |     |     | 210 |     |     |     |     |    |

|    | ccc | aac      | ctg | att | cat | gag | cct | ctt | gac | caa | ggc | aac | tgt | gca | ggc | tcc | 786  |
|----|-----|----------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|    | Pro | Asn      | Leu | Ile | His | Glu | Pro | Leu | Asp | Gln | Gly | Asn | Cys | Ala | Gly | Ser |      |
|    |     | 215      |     |     |     |     | 220 |     |     |     |     | 225 |     |     |     |     |      |
|    | tgg | gcc      | ttc | tcc | aca | gca | gct | gtg | gca | tcc | gat | cgt | gtc | tca | atc | cat | 834  |
| 5  | Trp | Ala      | Phe | Ser | Thr | Ala | Ala | Val | Ala | Ser | Asp | Arg | Val | Ser | Ile | His |      |
|    | 230 |          |     |     |     | 235 |     |     |     |     | 240 |     |     |     |     | 245 |      |
|    | tct | ctg      | gga | cac | atg | acg | cct | gtc | ctg | tcg | ccc | cag | aac | ctg | ctg | tct | 882  |
|    | Şer | Leu      | Gly | His | Met | Thr | Pro | Val | Leu | Ser | Pro | Gln | Asn | Leu | Leu | Ser |      |
|    |     |          |     |     | 250 |     |     |     |     | 255 |     |     |     |     | 260 |     |      |
| 10 | tgt | gac      | acc | cac | cag | cag | cag | ggc | tgc | cgc | ggt | ggg | cgt | ctc | gat | ggt | 930  |
|    | Cys | Asp      | Thr | His | Gln | Gln | Gln | Gly | Cys | Arg | Gly | Gly | Arg | Leu | Asp | Gly |      |
|    |     |          |     | 265 |     |     |     |     | 270 |     |     |     |     | 275 |     |     |      |
|    | gcc | :<br>tgg | tgg | ttc | ctg | cgt | cgc | cga | ggg | gtg | gtg | tct | gac | cac | tgc | tac | 978  |
|    | Ala | Trp      | Trp | Phe | Leu | Arg | Arg | Arg | Gly | Val | Val | Ser | Asp | His | Cys | Tyr |      |
| 15 |     |          | 280 |     |     |     |     | 285 |     |     |     |     | 290 |     |     |     |      |
|    | ccc | ttc      | tcg | ggc | cgt | gaa | cga | gac | gag | gct | ggc | cct | gcg | ccc | ccc | tgt | 1026 |
|    | Pro | Phe      | Ser | Gly | Arg | Glu | Arg | Asp | Glu | Ala | Gly | Pro | Ala | Pro | Pro | Cys |      |
|    |     | 295      |     |     |     |     | 300 |     |     |     |     | 305 |     |     |     |     |      |
|    | atg | atg      | cac | agc | cga | gcc | atg | ggt | cgg | ggc | aag | cgc | cag | gcc | act | gcc | 1074 |
| 20 | Met | Met      | His | Ser | Arg | Ala | Met | Gly | Arg | Gly | Lys | Arg | Gln | Ala | Thr | Ala |      |
|    | 310 |          |     |     |     | 315 |     |     |     |     | 320 |     |     |     |     | 325 |      |
|    | cac | tgc      | ccc | aac | agc | tat | gtt | aat | aac | aat | gac | atc | tac | cag | gtc | act | 1122 |
|    | His | Cys      | Pro | Asn | Ser | Tyr | Val | Asn | Asn | Asn | Asp | Ile | Tyr | Gln | Val | Thr |      |
|    |     |          |     |     | 330 |     |     |     |     | 335 | _   |     | =   |     | 340 |     |      |
| 25 | cct | gtc      | tac | cgc | ctc | ggc | tcc | aac | gac | aag | gag | atc | atg | aag | gag | ctg | 1170 |
|    |     |          |     |     |     |     |     |     | -   | _   |     |     | _   | _   |     | _   | -    |

|    | Pro  | Val  | Tyr   | Arg   | Leu   | Gly   | Ser  | Asn   | Asp   | Lys  | Glu  | Ile  | Met   | Lys   | Glu  | Leu   |      |
|----|------|------|-------|-------|-------|-------|------|-------|-------|------|------|------|-------|-------|------|-------|------|
|    |      |      |       | 345   |       |       |      |       | 350   |      |      |      |       | 355   |      |       |      |
|    | atg  | gag  | aat   | ggc   | cct   | gtc   | caa  | gcc   | ctc   | atg  | gag  | gtg  | cat   | gag   | gac  | ttc   | 1218 |
|    | Met  | Glu  | Asn   | Gly   | Pro   | Val   | Gln  | Ala   | Leu   | Met  | Glu  | Val  | His   | Glu   | Asp  | Phe   |      |
| 5  |      |      | 360   |       |       |       |      | 365   |       |      |      |      | 370   |       |      |       |      |
|    | ttc  | cta  | tac   | aag   | gga   | ggc   | atc  | tac   | agc   | cac  | acg  | cca  | gtg   | agc   | ctt  | ggg   | 1266 |
|    | Phe  | Leu  | Tyr   | Lys   | Gly   | Gly   | Ile  | Tyr   | Ser   | His  | Thr  | Pro  | Val   | Ser   | Leu  | Gly   |      |
|    |      | 375  |       |       |       |       | 380  |       |       |      |      | 385  |       |       |      |       |      |
|    | agg  | cca  | gag   | aga   | tac   | cgc   | cgg  | cat   | ggg   | acc  | cac  | tca  | gtc   | aag   | atc  | aca   | 1314 |
| 10 | Arg  | Pro  | Glu   | Arg   | Tyr   | Arg   | Arg  | His   | Gly   | Thr  | His  | Ser  | Val   | Lys   | Ile  | Thr   |      |
|    | 390  |      |       |       |       | 395   |      |       |       |      | 400  |      |       |       |      | 405   |      |
|    | gga  | tgg  | gga   | gag   | gag   | acg   | ctg  | cca   | gat   | gga  | agg  | acg  | ctc   | aaa   | tac  | tgg   | 1362 |
|    | Gly  | Trp  | Gly   | Glu   | Glu   | Thr   | Leu  | Pro   | Asp   | Gly  | Arg  | Thr  | Leu   | Lys   | Tyr  | Trp   |      |
|    |      |      |       |       | 410   |       |      |       |       | 415  |      |      |       |       | 420  |       |      |
| 15 | act  | gcg  | ġcc   | aac   | tcc   | tgg   | ggc  | cca   | gcc   | tgg  | ggc  | gag  | agg   | ggc   | cac  | ttc   | 1410 |
|    | Thr  | Ala  | Ala   | Asn   | Ser   | Trp   | Gly  | Pro   | Ala   | Trp  | Gly  | Glu  | Arg   | Gly   | His  | Phe   |      |
|    |      |      |       | 425   |       |       |      |       | 430   |      |      |      |       | 435   |      |       |      |
|    | cgc  | atc  | gtg   | cgc   | ggc   | gtc   | aat  | gag   | tgc   | gac  | atc  | gag  | agc   | ttc   | gtg  | ctg   | 1458 |
|    | Arg  | Ile  | Val   | Arg   | Gly   | Val   | Asn  | Glu   | Cys   | Asp  | Ile  | Glu  | Ser   | Phe   | Val  | Leu   |      |
| 20 |      |      | 440   |       |       |       |      | 445   |       |      |      |      | 450   |       |      |       |      |
|    | ggc  | gtc  | tgg   | ggc   | cgc   | gtg   | ggc  | atg   | gag   | gac  | atg  | ggt  | cat   | cac   | tga  |       | 1503 |
|    | Gly  | Val  | Trp   | Gly   | Arg   | Val   | Gly  | Met   | Glu   | Asp  | Met  | Gly  | His   | His   |      |       |      |
|    |      | 455  |       |       |       |       | 460  |       |       |      | •    | 465  |       |       |      |       |      |
|    | ggct | gege | gc a  | accad | gege  | ıg gt | ccgg | gcctg | g gga | tcca | ggc  | taac | iggco | gg c  | ggaa | gaggc | 1563 |
| 25 | ccca | atgo | igg d | ggtg  | jacco | c ag  | ccto | gcco  | gac   | agag | jccc | gggg | cgca  | igg c | gggc | gccag | 1623 |

#### 328/346

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cgagactggc ggagcccca gacctcccag tggggacggg gcagggcctg gcctgggaag 1743

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cctccgactc ctgggttcaa gtgaccctcc cacctcagcc tctcaagtag ctgggactac 1983

aggtgcacca ccacacctgg ctaatttttg tatttttgt aaagaggggg gtctcactgt 2043

gttgcccagg ctggtctcga actcctgggc tcaagcggtc cacctgcctc cgcctcccaa 2103

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geeegeteet gteeeegaca teaegtgtat teegeaegte eeeteegege tgtgtgteta 180
etgagaeggg gaggegtgae agggeeeggg teeettetea gtggtgetet gtgetteagg 240

|    | gca | agct | ccc | cgtc  | tccg | gg c | gcac | ttcc  | c to | gcct | gtgt | tcg | gtcc | atc | ctcc | tttctc | 300 |
|----|-----|------|-----|-------|------|------|------|-------|------|------|------|-----|------|-----|------|--------|-----|
|    | cag | cctc | ctc | ccct  | cgca | gg t | ggga | tcgt  | c gg | tggg | accg | gag | cgcg | ggc | gggc | geggee | 360 |
|    | ccc | cggg | acc | atg ( | gcc  | ggg  | tcc  | gac   | acc  | gcg  | ccc  | ttc | ctc  | agc | cag  | gcg    | 409 |
|    |     |      |     | Met 1 | Ala  | Gly  | Ser  | Asp ' | Thr  | Ala  | Pro  | Phe | Leu  | Ser | Gln  | Ala    |     |
| 5  |     |      |     | 1     |      |      |      | 5     |      |      |      |     | 10   |     |      |        |     |
|    | gat | gac  | ccg | gac   | gac  | ggg  | cca  | gtg   | cct  | ggc  | acc  | ccg | ggg  | ttg | cca  | ggg    | 457 |
|    | Asp | Asp  | Pro | Asp   | Asp  | Gly  | Pro  | Val   | Pro  | Gly  | Thr  | Pro | Gly  | Leu | Pro  | Gly    |     |
|    |     | 15   |     |       |      |      | 20   |       |      |      |      | 25  |      |     |      |        |     |
|    | tcc | acg  | ggg | aac   | ccg  | aag  | tcc  | gag   | gag  | ccc  | gag  | gto | ccg  | gac | cag  | gag    | 505 |
| 10 | Ser | Thr  | Gly | Asn   | Pro  | Lys  | Ser  | Glu   | Glu  | Pro  | Glu  | Val | Pro  | Asp | Gln  | Glu    |     |
|    | 30  |      |     |       |      | 35   |      |       |      |      | 40   |     |      |     |      | 45     |     |
|    | ggg | ctg  | cag | cgc   | atc  | acc  | ggc  | ctg   | tct  | ccc  | ggc  | cgt | tcg  | gct | ctc  | ata -  | 553 |
|    | Gly | Leu  | Gln | Arg   | Ile  | Thr  | Gly  | Leu   | Ser  | Pro  | Gly  | Arg | Ser  | Ala | Leu  | Ile    |     |
|    |     |      |     |       | 50   |      |      |       |      | 55   |      |     |      |     | 60   |        |     |
| 15 | gtg | gcg  | gtg | ctg   | tgc  | tac  | atc  | aat   | ctc  | ctg  | aac  | tac | atg  | gac | cgc  | ttc    | 601 |
|    | Val | Ala  | Val | Leu   | Cys  | Tyr  | Ile  | Asn   | Leu  | Leu  | Asn  | Tyr | Met  | Asp | Arg  | Phe    |     |
|    |     |      |     | 65    |      |      |      |       | 70   |      |      |     |      | 75  |      |        |     |
|    | acc | gtg  | gct | ggc   | gtc  | ctt  | ccc  | gac   | atc  | gag  | cag  | ttc | ttc  | aac | atc  | ggg    | 649 |
|    | Thr | Val  | Ala | Gly   | Val  | Leu  | Pro  | Asp   | Ile  | Glu  | Gln  | Phe | Phe  | Asn | Ile  | Gly    |     |
| 20 |     |      | 80  |       |      |      |      | 85    |      |      |      |     | 90   |     |      |        |     |
|    | gac | agt  | agc | tct   | ggg  | ctc  | atc  | cag   | acc  | gtg  | ttc  | atc | tcc  | agt | tac  | atg    | 697 |
|    | Asp | Ser  | Ser | Ser   | Gly  | Leu  | Ile  | Gln   | Thr  | Val  | Phe  | Ile | Ser  | Ser | Tyr  | Met    |     |
|    |     | 95   |     |       |      |      | 100  |       |      |      |      | 105 |      |     |      |        |     |
|    | gtg | ttg  | gca | cct   | gtg  | ttt  | ggc  | tac   | ctg  | ggt  | gac  | agg | tac  | aat | cgg  | aag    | 745 |
| 25 | Val | Leu  | Ala | Pro   | Val  | Phe  | Gly  | Tyr   | Leu  | Gly  | Asp  | Arg | Tyr  | Asn | Arg  | Lys    |     |

|    | 110 |     |     |     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |      |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|    | tat | ctc | atg | tgc | ggg | ggc | att | gcc | ttc | tgg | tcc | ctg | gtg | aca | ctg | ggg | 793  |
|    | Tyr | Leu | Met | Cys | Gly | Gly | Ile | Ala | Phe | Trp | Ser | Leu | Val | Thr | Leu | Gly |      |
|    |     |     |     |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |      |
| 5  | tca | tcc | ttc | atc | ccc | gga | gag | cat | ttc | tgg | ctg | ctc | ctc | ctg | acc | cgg | 841  |
|    | Ser | Ser | Phe | Ile | Pro | Gly | Glu | His | Phe | Trp | Leu | Leu | Leu | Leu | Thr | Arg |      |
|    |     |     |     | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |      |
|    | ggc | ctg | gtg | ggg | gtc | ggg | gag | gcc | agt | tat | tcc | acc | atc | gcg | ccc | act | 889  |
|    | Gly | Leu | Val | Gly | Val | Gly | Glu | Ala | Ser | Tyr | Ser | Thr | Ile | Ala | Pro | Thr |      |
| 10 |     |     | 160 |     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |      |
|    | ctc | att | gcc | gac | ctc | ttt | gtg | gcc | gac | cag | cgg | agc | cgg | atg | ctc | agc | 937  |
|    | Leu | Ile | Ala | Asp | Leu | Phe | Val | Ala | Asp | Gln | Arg | Ser | Arg | Met | Leu | Ser |      |
|    |     | 175 |     |     |     |     | 180 |     |     |     |     | 185 |     |     |     | ,   |      |
|    | atc | ttc | tac | ttt | gcc | att | ccg | gtg | ggc | agt | ggt | ctg | ggc | tac | att | gca | 985  |
| 15 | Ile | Phe | Tyr | Phe | Ala | Ile | Pro | Val | Gly | Ser | Gly | Leu | Gly | Tyr | Ile | Ala |      |
|    | 190 |     |     |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |      |
|    | ggc | tcc | aaa | gtg | aag | gat | atg | gct | gga | gac | tgg | cac | tgg | gct | ctg | agg | 1033 |
|    | Gly | Ser | Lys | Val | Lys | Asp | Met | Ala | Gly | Asp | Trp | His | Trp | Ala | Leu | Arg |      |
|    |     |     |     |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |      |
| 20 | gtg | aca | ccg | ggt | cta | gga | gtg | gtg | gcc | gtt | ctg | ctg | ctg | ttc | ctg | gta | 1081 |
|    | Val | Thr | Pro | Gly | Leu | Gly | Val | Val | Ala | Val | Leu | Leu | Leu | Phe | Leu | Val |      |
|    |     |     |     | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |      |
|    | gtg | cgg | gag | ccg | cca | agg | gga | gcc | gtg | gag | cgc | cac | tca | gat | ttg | cca | 1129 |
|    | Val | Arg | Glu | Pro | Pro | Arg | Gly | Ala | Val | Glu | Arg | His | Ser | Asp | Leu | Pro |      |
| 25 |     |     | 240 |     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |      |

|    | ccc | ctg | aac | CCC | acc | tcg | tgg | tgg | gca | gat | ctg | agg | gct | ctg | gca | aga | 1177 |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|    | Pro | Leu | Asn | Pro | Thr | Ser | Trp | Trp | Ala | Asp | Leu | Arg | Ala | Leu | Ala | Arg |      |
|    |     | 255 |     |     |     |     | 260 |     |     |     |     | 265 |     |     |     |     |      |
|    | aat | ctc | atc | ttt | gga | ctc | atc | acc | tgc | ctg | acc | gga | gtc | ctg | ggt | gtg | 1225 |
| 5  | Asn | Leu | Ile | Phe | Gly | Leu | Ile | Thr | Cys | Leu | Thr | Gly | Val | Leu | Gly | Val |      |
|    | 270 |     |     |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |      |
|    | ggc | ctg | ggt | gtg | gag | atc | agc | cgc | cgg | ctc | cgc | cac | tcc | aac | ccc | cgg | 1273 |
|    | Gly | Leu | Gly | Val | Glu | Ile | Ser | Arg | Arg | Leu | Arg | His | Ser | Asn | Pro | Arg |      |
|    |     |     |     |     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |      |
| 10 | gct | gat | ccc | ctg | gtc | tgt | gcc | act | ggc | ctc | ctg | ggc | tct | gca | ccc | ttc | 1321 |
|    | Ala | Asp | Pro | Leu | Val | Cys | Ala | Thr | Gly | Leu | Leu | Gly | Ser | Ala | Pro | Phe |      |
|    |     |     |     | 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |     |      |
|    | ctc | ttc | ctg | tcc | ctt | gcc | tgc | gcc | cgt | ggt | agc | atc | gtg | gcc | act | tat | 1369 |
|    | Leu | Phe | Leu | Ser | Leu | Ala | Cys | Ala | Arg | Gly | Ser | Ile | Val | Ala | Thr | Tyr |      |
| 15 |     |     | 320 |     |     |     |     | 325 |     |     |     |     | 330 |     |     |     |      |
|    | att | ttc | atc | ttc | att | gga | gag | acc | ctc | ctg | tcc | atg | aac | tgg | gcc | atc | 1417 |
|    | Ile | Phe | Ile | Phe | Ile | Gly | Glu | Thr | Leu | Leu | Ser | Met | Asn | Trp | Ala | Ile |      |
|    |     | 335 |     |     |     |     | 340 |     |     |     |     | 345 |     |     |     |     |      |
|    | gtg | gcc | gac | att | ctg | ctg | tac | gtg | gtg | atc | cct | acc | cga | cgc | tcc | acc | 1465 |
| 20 | Val | Ala | Asp | Ile | Leu | Leu | Tyr | Val | Val | Ile | Pro | Thr | Arg | Arg | Ser | Thr |      |
|    | 350 |     |     |     |     | 355 |     |     |     |     | 360 |     |     |     |     | 365 |      |
|    | gcc | gag | gcc | ttc | cag | atc | gtg | ctg | tcc | cac | ctg | ctg | ggt | gat | gct | ggg | 1513 |
|    | Ala | Glu | Ala | Phe | Gln | Ile | Val | Leu | Ser | His | Leu | Leu | Gly | Asp | Ala | Gly |      |
|    |     |     |     |     | 370 |     |     |     |     | 375 |     |     |     |     | 380 |     |      |
| 25 | agc | ccc | tac | ctc | att | ggc | ctg | atc | tct | gac | cgc | ctg | cgc | cgg | aac | tgg | 1561 |

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|    | Ser  | Pro  | Tyr   | Leu  | Ile  | Gly   | Leu   | Ile  | Ser   | Asp  | Arg  | Leu  | Arg   | Arg   | Asn  | Trp   |      |
|----|------|------|-------|------|------|-------|-------|------|-------|------|------|------|-------|-------|------|-------|------|
|    |      |      |       | 385  |      |       |       |      | 390   |      |      |      |       | 395   |      |       |      |
|    | ccc  | ccc  | tcc   | ttc  | ttg  | tcc   | gag   | ttc  | cgg   | gct  | ctg  | cag  | ttc   | tcg   | ctc  | atg   | 1609 |
|    | Pro  | Pro  | Ser   | Phe  | Leu  | Ser   | Glu   | Phe  | Arg   | Ala  | Leu  | Gln  | Phe   | Ser   | Leu  | Met   |      |
| 5  |      |      | 400   |      |      |       |       | 405  |       |      |      |      | 410   |       |      |       |      |
|    | ctc  | tgc  | gcg   | ttt  | gtt  | ggg   | gca   | ctg  | ggc   | ggc  | gca  | gcc  | ttc   | ctg   | ggc  | acc   | 1657 |
|    | Leu  | Cys  | Ala   | Phe  | Val  | Gly   | Ala   | Leu  | Gly   | Gly  | Ala  | Ala  | Phe   | Leu   | Gly  | Thr   |      |
|    |      | 415  |       |      |      |       | 420   |      |       |      |      | 425  |       |       |      |       |      |
|    | gcc  | atc  | ttc   | att  | gag  | gcc   | gac   | cgc  | cgg   | cgg  | gca  | cag  | ctg   | cac   | gtg  | cag   | 1705 |
| 10 | Ala  | Ile  | Phe   | Ile  | Glu  | Ala   | Asp   | Arg  | Arg   | Arg  | Ala  | Gln  | Leu   | His   | Val  | Gln   |      |
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|    | ggc  | ctg  | ctg   | cac  | gaa  | gca   | ggg   | tcc  | aca   | gac  | gac  | cgg  | att   | gtg   | gtg  | ccc   | 1753 |
|    | Gly  | Leu  | Leu   | His  | Glu  | Ala   | Gly   | Ser  | Thr   | Asp  | Asp  | Arg  | Ile   | Val   | Val  | Pro   |      |
|    |      |      |       |      | 450  |       |       |      |       | 455  |      |      |       |       | 460  |       |      |
| 15 | cag  | cgg  | ggc   | cgc  | tcc  | acc   | cgc   | gtg  | ccc   | gtg  | gcc  | agt  | gtg   | ctc   | atc  | tga   | 1801 |
|    | Gln  | Arg  | Gly   | Arg  | Ser  | Thr   | Arg   | Val  | Pro   | Val  | Ala  | Ser  | Val   | Leu   | Ile  |       |      |
|    |      |      |       | 465  |      |       |       |      | 470   |      |      |      |       | 475   |      |       |      |
|    | gagg | ctgo | cg c  | tcac | ctac | c to  | rcaca | tctg | cca   | cago | tgg: | ccct | gggc  | cc a  | cccc | acgaa | 1861 |
|    | gggc | ctgg | ige c | taac | ccct | t gg  | ccto  | gccc | ago   | ttcc | aga  | ggga | ıccct | gg g  | ccgt | gtgcc | 1921 |
| 20 | agct | ccca | iga c | acta | cato | ıg gt | agct  | cago | gga   | ggag | igtg | gggg | tcca  | igg a | gggg | gatcc | 1981 |
|    | ctct | ccac | ag g  | ggca | gccc | c aa  | ıgggc | tegg | , tgc | tatt | tgt  | aacg | gaat  | aa a  | attt | gtagc | 2041 |
|    | cag  |      |       |      |      |       |       |      |       |      |      |      |       |       |      |       | 2044 |
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333/346

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caggeggegg caggegggea agegggeggg tgeegeagee eaggeeeggg tegegeetet 180

ttgttteeae gggtagegge geagteeegg geeeegggeg gaagtgagae gegeteggeg 240

cgggggeege ggeggeegea ee atg age gae ate ege eac teg etg ege 292

Met Ser Asp Ile Arg His Ser Leu Leu Arg

15 1 5 10

cgc gat gcg ctg agc gcc gcc aag gag gtg ttg tac cac ctg gac atc 340 Arg Asp Ala Leu Ser Ala Ala Lys Glu Val Leu Tyr His Leu Asp Ile

15 20 25

tac ttc agc agc cag ctg cag agc gcg ccg ctg ccc atc gtg gac aag 388

20 Tyr Phe Ser Ser Gln Leu Gln Ser Ala Pro Leu Pro Ile Val Asp Lys

30 35 40

ggc ccc gtg gag ctg ctg gag gag ttc gtg ttc cag gtg ccc aag gag 436 Gly Pro Val Glu Leu Leu Glu Glu Phe Val Phe Gln Val Pro Lys Glu

45 50 55

25 cgc agc gcg cag ccc aag aga ctg aat tcc ctt cag gag ctt caa ctt 484

|    | Arg | Ser | Ala | Gln | Pro | Ъуs | Arg | Leu | Asn | Ser | Leu | Gln | Glu | Leu | Gln | Leu |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    |     | 60  |     |     |     |     | 65  |     |     |     |     | 70  |     |     |     |     |     |
|    | ctt | gaa | atc | atg | tgc | aat | tat | ttc | cag | gag | caa | acc | aag | gac | tct | gtt | 532 |
|    | Leu | Glu | Ile | Met | Суз | Asn | Tyr | Phe | Gln | Glu | Gln | Thr | Lys | Asp | Ser | Val |     |
| 5  | 75  |     |     |     |     | 80  |     |     |     |     | 85  |     |     |     |     | 90  |     |
|    | cgg | cag | att | att | ttt | tca | tcc | ctt | ttc | agc | cct | caa | ggg | aac | aaa | gcc | 580 |
|    | Arg | Gln | Ile | Ile | Phe | Ser | Ser | Leu | Phe | Ser | Pro | Gln | Gly | Asn | Lys | Ala |     |
|    |     |     |     |     | 95  |     |     |     |     | 100 |     |     |     |     | 105 |     |     |
|    | gat | gac | agc | cgg | atg | agc | ttg | ttg | gga | aaa | ctg | gtc | tcc | atg | gcg | gtg | 628 |
| 10 | Asp | Asp | Ser | Arg | Met | Ser | Leu | Leu | Gly | Lys | Leu | Val | Ser | Met | Ala | Val |     |
|    |     |     |     | 110 |     |     |     |     | 115 |     |     |     |     | 120 |     |     |     |
|    | gct | gtg | tgt | cga | atc | ccg | gtg | ttg | gag | tgt | gct | gcc | tcc | tgg | ctt | cag | 676 |
|    | Ala | Val | Cys | Arg | Ile | Pro | Val | Leu | Glu | Cys | Ala | Ala | Ser | Trp | Leu | Gln |     |
|    |     |     | 125 |     |     |     |     | 130 |     |     |     |     | 135 |     |     |     |     |
| 15 | cgg | acg | ccc | gtg | gtt | tac | tgt | gtg | agg | tta | gcc | aag | gcc | ctt | gta | gat | 724 |
|    | Arg | Thr | Pro | Val | Val | Tyr | Cys | Val | Arg | Leu | Ala | Lys | Ala | Leu | Val | Asp |     |
|    |     | 140 |     |     |     |     | 145 |     |     |     |     | 150 |     |     |     |     |     |
|    | gac | tac | tgc | tgt | ttg | gtg | ccg | gga | tcc | att | cag | acg | ctg | aag | cag | ata | 772 |
|    | Asp | Tyr | Cys | Cys | Leu | Val | Pro | Gly | Ser | Ile | Gln | Thr | Leu | Lys | Gln | Ile |     |
| 20 | 155 |     |     |     |     | 160 |     |     |     |     | 165 |     |     |     |     | 170 |     |
|    | ttc | agt | gcc | agc | ccg | aga | ttc | tgc | tgc | cag | ttc | atc | acc | tcc | gtt | acc | 820 |
|    | Phe | Ser | Ala | Ser | Pro | Arg | Phe | Cys | Cys | Gln | Phe | Ile | Thr | Ser | Val | Thr |     |
|    |     |     |     |     | 175 |     |     |     |     | 180 |     |     |     |     | 185 |     |     |
|    | gcg | ctc | tat | gac | ctg | tca | tca | gat | gac | ctc | att | cca | cct | atg | gac | ttg | 868 |
| 25 | Ala | Leu | Tyr | Asp | Leu | Ser | Ser | Asp | Asp | Leu | Ile | Pro | Pro | Met | Asp | Leu |     |

|    |     |     |     | 190 |     |     |     |     | 195 |     |     |     |     | 200 |     |     |      |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|    | ctt | gaa | atg | att | gtc | acc | tgg | att | ttt | gag | gac | cca | agg | ttg | att | ctc | 916  |
|    | Leu | Glu | Met | Ile | Val | Thr | Trp | Ile | Phe | Glu | Asp | Pro | Arg | Leu | Ile | Leu |      |
|    |     |     | 205 |     |     |     |     | 210 |     |     |     |     | 215 |     |     |     |      |
| 5  | atc | act | ttt | tta | aat | act | ccg | att | gcg | gcc | aat | ctg | cca | ata | gga | ttc | 964  |
|    | Ile | Thr | Phe | Leu | Asn | Thr | Pro | Ile | Ala | Ala | Asn | Leu | Pro | Ile | Gly | Phe |      |
|    |     | 220 |     |     |     |     | 225 |     |     |     |     | 230 |     |     |     |     |      |
|    | tta | gag | ctc | acc | ccg | ctc | gtt | gga | ttg | atc | cgc | tgg | tgc | gtg | aag | gca | 1012 |
|    | Leu | Glu | Leu | Thr | Pro | Leu | Val | Gly | Leu | Ile | Arg | Trp | Cys | Val | Lys | Ala |      |
| 10 | 235 |     |     |     |     | 240 |     |     |     |     | 245 |     |     |     |     | 250 |      |
|    | ccc | ctg | gct | tat | aaa | agg | aaa | aag | aag | ccc | ccc | tta | tcc | aat | ggc | cat | 1060 |
|    | Pro | Leu | Ala | Tyr | Lys | Arg | Lys | Lys | Lys | Pro | Pro | Leu | Ser | Asn | Gly | His |      |
|    |     |     |     |     | 255 |     |     |     |     | 260 |     |     |     |     | 265 |     |      |
|    | gtc | agc | aac | aag | gtc | aca | aag | gac | ccg | ggc | gtg | ggg | atg | gac | aga | gac | 1108 |
| 15 | Val | Ser | Asn | Lys | Val | Thr | Lys | Asp | Pro | Gly | Val | Gly | Met | Asp | Arg | Asp |      |
|    |     |     |     | 270 |     |     |     |     | 275 |     |     |     |     | 280 |     |     |      |
|    | tcc | cac | ctc | ttg | tac | tca | aaa | ctc | cac | ctc | agc | gtc | ctg | caa | gtg | ctc | 1156 |
|    | Ser | His | Leu | Leu | Tyr | Ser | Lys | Leu | His | Leu | Ser | Val | Leu | Gln | Val | Leu |      |
|    |     |     | 285 |     |     |     |     | 290 |     |     |     |     | 295 |     |     |     |      |
| 20 | atg | acg | ctg | cag | ctg | cac | ctg | acc | gag | aag | aat | ctg | tat | ggg | cgc | ctg | 1204 |
|    | Met | Thr | Leu | Gln | Leu | His | Leu | Thr | Glu | Lys | Asn | Leu | Tyr | Gly | Arg | Leu |      |
|    |     | 300 |     |     |     |     | 305 |     |     |     |     | 310 |     |     |     |     |      |
|    | ggg | ctg | atc | ctc | ttc | gac | cac | atg | gtc | ccg | ctg | gta | gag | gag | atc | aac | 1252 |
|    | Gly | Leu | Ile | Leu | Phe | Asp | His | Met | Val | Pro | Leu | Val | Glu | Glu | Ile | Asn |      |
| 25 | 315 |     |     |     |     | 320 |     |     |     |     | 325 |     |     |     |     | 330 |      |

|    | agg  | ttg   | gcg  | gat  | gaa  | ctg  | aac  | ccc  | ctc   | aac  | gcc  | tcc   | cag  | gag   | att   | gag   | 1300 |
|----|------|-------|------|------|------|------|------|------|-------|------|------|-------|------|-------|-------|-------|------|
|    | Arg  | Leu   | Ala  | Asp  | Glu  | Leu  | Asn  | Pro  | Leu   | Asn  | Ala  | Ser   | Gln  | Glu   | Ile   | Glu   |      |
|    |      |       |      |      | 335  |      |      |      |       | 340  |      |       |      |       | 345   |       |      |
|    | ctc  | tcg   | ctg  | gac  | cgg  | ctg  | gcg  | cag  | gct   | ctg  | cag  | gtg   | gcc  | atg   | gcc   | tca   | 1348 |
| 5  | Leu  | Ser   | Leu  | Asp  | Arg  | Leu  | Ala  | Gln  | Ala   | Leu  | Gln  | Val   | Ala  | Met   | Ala   | Ser   |      |
|    |      |       |      | 350  |      |      |      |      | 355   |      |      |       |      | 360   |       |       |      |
|    | gga  | gct   | ctg  | ctg  | tgc  | acg  | aga  | gat  | gac   | .ctg | aga  | acc   | ttg  | tgc   | tcc   | agg   | 1396 |
|    | Gly  | Ala   | Leu  | Leu  | Cys  | Thr  | Arg  | Asp  | Asp   | Leu  | Arg  | Thr   | Leu  | Cys   | Ser   | Arg   |      |
|    |      |       | 365  |      |      |      |      | 370  |       |      |      |       | 375  |       |       |       |      |
| 10 | ctg  | ccc   | cat  | aat  | aac  | ctc  | ctc  | cag  | ctg   | gtg  | atc  | tcg   | ggt  | ccc   | gtg   | cag   | 1444 |
|    | Leu  | Pro   | His  | Asn  | Asn  | Leu  | Leu  | Gln  | Leu   | Val  | Ile  | Ser   | Gly  | Pro   | Val   | Gln   |      |
|    |      | 380   |      |      |      |      | 385  |      |       |      |      | 390   |      |       |       |       |      |
|    | cag  | tcg   | cct  | cac  | gcc  | gcg  | ctc  | CCC  | ccg   | ggg  | ttc  | tac   | ccc  | cac   | atc   | cac   | 1492 |
|    | Gln  | Ser   | Pro  | His  | Ala  | Ala  | Leu  | Pro  | Pro   | Gly  | Phe  | Tyr   | Pro  | His   | Ile   | His   |      |
| 15 | 395  |       |      |      |      | 400  |      |      |       |      | 405  |       |      |       |       | 410   |      |
|    | acg  | ccc   | ccg  | ctg  | ggc  | tac  | ggg  | gct  | gtc   | ccg  | gcc  | cac   | ccc  | gcc   | gcc   | cac   | 1540 |
|    | Thr  | Pro   | Pro  | Leu  | Gly  | Tyr  | Gly  | Ala  | Val   | Pro  | Ala  | His   | Pro  | Ala   | Ala   | His   |      |
|    |      |       |      |      | 415  |      |      |      |       | 420  |      |       |      |       | 425   |       |      |
|    | ccc  | gcc   | ctg  | ccc  | acg  | cac  | ccc  | ggc  | cac   | acc  | ttc  | atc   | tcc  | ggc   | gtg   | acc   | 1588 |
| 20 | Pro  | Ala   | Leu  | Pro  | Thr  | His  | Pro  | Gly  | His   | Thr  | Phe  | Ile   | Ser  | Gly   | Val   | Thr   |      |
|    |      |       |      | 430  |      |      |      |      | 435   |      |      |       |      | 440   |       |       |      |
|    | ttt  | ccc   | ttc  | agg  | ccc  | atc  | cgc  | tag  | gcto  | gcco | gt g | ıtgtg | cctt | c to  | jeget | ctcg  | 1642 |
|    | Phe  | Pro   | Phe  | Arg  | Pro  | Ile  | Arg  |      |       |      |      |       |      |       |       |       |      |
|    | ٠    |       | 445  |      |      |      |      | 450  |       |      |      |       |      |       |       |       |      |
| 25 | ctgg | jacga | ag c | cttt | cgae | a to | gaac | gaat | : aac | caaa | ctc  | ccad  | aada | ıga a | ccto  | aggga | 1702 |

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aggggteggg cagecetee cegeeggeag aacegtettg gtgteaegga gteeaggtge 1762
tteecaeeeg gtegeattet ttgacatgea gattggatgg tggagggaag agteeageet 1822
ctgeeggagg cetgetgegt geattttaa aagatgeega teetgggage etetgttete 1882
tgegeattte agacaeagee tgtgtggega ggagtgtgae ggeaggagee aegggtgeaa 1942
geeegtgtgt etggeetett teetegtgaa gaegatgtgt eeeegeeaga aaaagtggge 2002
teettetgea geeeegtgag etgageeeag getgegtagt gaeeaeaage ttatgtgeag 2062
caetgeteag ggaggetgte aggaatteee eteaeetegg aaaggaaeett eteagttta 2122
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15 <220>

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<222> (16)..(333)

<400> 148

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Met Arg Arg Ile Ser Leu Thr Ser Ser Pro Val Arg

1 5 10

ctt ctt ttg ttt ctg ctg ttg cta cta ata gcc ttg gag atc atg gtt 99
Leu Leu Leu Phe Leu Leu Leu Leu Ile Ala Leu Glu Ile Met Val

25 15 20 25

|    | ggt  | ggt   | cac   | tct   | ctt   | tgc   | ttc   | aac   | ttc   | act   | ata  | aaa  | tca   | ttg   | tcc   | aga    | 147 |
|----|------|-------|-------|-------|-------|-------|-------|-------|-------|-------|------|------|-------|-------|-------|--------|-----|
|    | Gly  | Gly   | His   | Ser   | Leu   | Cys   | Phe   | Asn   | Phe   | Thr   | Ile  | Lys  | Ser   | Leu   | Ser   | Arg    |     |
|    |      | 30    |       |       |       |       | 35    |       |       |       |      | 40   |       |       |       |        |     |
|    | cct  | gga   | cag   | ccc   | tgg   | tgt   | gaa   | gcg   | cag   | gtc   | ttc  | ttg  | aat   | aaa   | aat   | ctt    | 195 |
| 5  | Pro  | Gly   | Gln   | Pro   | Trp   | Cys   | Glu   | Ala   | Gln   | Val   | Phe  | Leu  | Asn   | Lys   | Asn   | Leu    |     |
|    | 45   |       |       |       |       | 50    |       |       |       |       | 55   |      |       |       |       | 60     |     |
|    | ttc  | ctt   | cag   | tac   | aac   | agt   | gac   | aac   | aac   | atg   | gtc  | aaa  | cct   | ctg   | ggc   | ctc    | 243 |
|    | Phe  | Leu   | Gln   | Tyr   | Asn   | Ser   | Asp   | Asn   | Asn   | Met   | Val  | Lys  | Pro   | Leu   | Gly   | Leu    |     |
|    |      |       |       |       | 65    |       |       |       |       | 70    |      |      |       |       | 75    |        |     |
| 10 | ctg  | ggg   | aag   | aag   | gta   | aat   | gcc   | acc   | agc   | act   | tgg  | gga  | gaa   | aac   | сса   | aac    | 291 |
|    | Leu  | Gly   | Lys   | Lys   | Val   | Asn   | Ala   | Thr   | Ser   | Thr   | Trp  | Gly  | Glu   | Asn   | Pro   | Asn    |     |
|    |      |       |       | 80    |       |       |       |       | 85    |       | ·    |      |       | 90    |       |        |     |
|    | gct  | ggg   | aga   | agt   | ggg   | gcg   | aga   | cct   | cag   | gat   | gct  | cct  | ttg   | tga   |       |        | 333 |
| •  | Ala  | Gly   | Arg   | Ser   | Gly   | Ala   | Arg   | Pro   | Gln   | Asp   | Ala  | Pro  | Leu   |       |       |        |     |
| 15 |      |       | 95    |       |       |       |       | 100   |       |       |      |      | 105   |       |       |        |     |
|    | cato | caaac | ccc c | cagat | aaaç  | ja co | cagto | gated | tto   | cact  | ctg  | caag | gtcga | aga t | gttt  | tgtca  | 393 |
|    | acgt | gaag  | gca ç | gaac  | gtg   | ca ct | ggt   | gcato | cto   | gcag  | gttc | gcca | accaa | atg ( | gagag | gaaatc | 453 |
|    | cctc | ctct  | tt g  | gacgo | caato | ga ac | catga | accto | gac   | agta  | att  | aato | catga | ag o  | ccagt | aagat  | 513 |
|    | caag | gaga  | aca t | ggaa  | agaaa | ng ac | cagag | gggct | gga   | aaag  | gtat | ttca | aggaa | agc t | tctca | aaggg  | 573 |
| 20 | agac | tgcg  | gat c | cacto | gcto  | a gg  | ggaat | tctt  | ago   | gcac  | etgg | gagg | gcaat | gc (  | cagaa | ccgac  | 633 |
|    | aggo | agaa  | aga t | ccad  | ctag  | ga gg | gtgat | acca  | cgç   | cggc  | gca  | gagt | tgtt  | ca o  | cctgt | ggtcc  | 693 |
|    | tcga | tcgc  | etg a | acago | ctto  | g ct  | ccca  | actgo | : tgt | gtgt  | tcc  | ctga | agtca | ag t  | ggag  | gcgga  | 753 |
|    | gcct | gcaa  | atg a | agcgg | gagat | c go  | egect | ctgo  | att   | ccaç  | gtct | tgg  | caaca | aga 🤅 | caac  | jactcc | 813 |
|    | gtct | caaa  | aaa a | aaaa  | attt  | t tt  | ttca  | agtac | ata   | tttt  | tta  | aaag | gatag | gg (  | ctggg | gcacag | 873 |
| 25 | cago | tcac  | cat o | ctata | atco  | c aa  | acact | ttac  | a aac | racct | aaa  | cago | ragga | atc a | actto | agccc  | 933 |

aggaatetga agetgeagtg ageetttget egtgagattg tggaeetatg ateetaceae 993
cageecacet ggttetaaca ecceeteete tatgtgtgag agggagagaa gaaaagtgag 1053
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<213> Homo sapiens

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<400> 149

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tegtetteae aggegaeeae geaceaeaea cactaaeagt egtetteaea ggegaeegeg 180
caccacacae actaaeggae gtgeeegaea tetteaeagg cacage atg age cet 235

Met Ser Pro

|    | gat  | gtg   | cgc   | ttt   | ctg   | ctc   | ctg   | ctc   | ctg   | ctc   | ctg  | CCC  | ctt   | cgg   | agg   | cct    | 283  |
|----|------|-------|-------|-------|-------|-------|-------|-------|-------|-------|------|------|-------|-------|-------|--------|------|
|    | Asp  | Val   | Arg   | Phe   | Leu   | Leu   | Leu   | Leu   | Leu   | Leu   | Leu  | Pro  | Leu   | Arg   | Arg   | Pro    |      |
|    |      | 5     |       |       |       |       | 10    |       |       |       |      | 15   |       |       |       |        |      |
|    | gtg  | cca   | gtg   | gca   | gct   | ggg   | ccc   | gga   | gac   | acc   | agg  | ccg  | gca   | ctg   | ctc   | tct    | 331  |
| 5  | Val  | Pro   | Val   | Ala   | Ala   | Gly   | Pro   | Gly   | Asp   | Thr   | Arg  | Pro  | Ala   | Leu   | Leu   | Ser    |      |
|    | 20   |       |       |       |       | 25    |       | •     |       |       | 30   |      |       |       |       | 35     |      |
|    | ttc  | gag   | gca   | ccc   | gtg   | ttt   | gtg   | ccg   | acg   | ctg   | act  | ccc  | ggt   | tgt   | ctg   | cag    | 379  |
|    | Phe  | Glu   | Ala   | Pro   | Val   | Phe   | Val   | Pro   | Thr   | Leu   | Thr  | Pro  | Gly   | Cys   | Leu   | Gln    |      |
|    |      |       |       |       | 40    |       |       |       |       | 45    |      |      |       |       | 50    |        |      |
| 10 | cag  | cca   | cgt   | ggc   | cga   | aat   | gga   | gcc   | tct   | cca   | cgg  | ggg  | ctc   | ctt   | ccc   | cag    | 427  |
|    | Gln  | Pro   | Arg   | Gly   | Arg   | Asn   | Gly   | Ala   | Ser   | Pro   | Arg  | Gly  | Leu   | Leu   | Pro   | Gln    |      |
|    |      |       |       | 55    |       |       |       |       | 60    |       |      |      |       | 65    |       |        |      |
|    | ccc  | ctg   | gat   | ggc   | aca   | gca   | gcc   | tct   | cct   | gtc   | tgt  | cac  | cac   | gtg   | tga   |        | 472  |
|    | Pro  | Leu   | Asp   | Gly   | Thr   | Ala   | Ala   | Ser   | Pro   | Val   | Cys  | His  | His   | Val   |       |        |      |
| 15 |      |       | 70    |       |       |       |       | 75    |       |       |      |      | 80    |       |       |        |      |
|    | ccto | ctco  | cct t | agto  | ttca  | ig co | gcto  | catco | acg   | rtctg | jcag | gggg | atct  | aa (  | ctctg | ıtccca | 532  |
|    | gggt | atco  | cca ç | jacco | etgge | t ca  | cgc   | ccag  | g gct | ctcc  | att  | cago | gctco | at (  | cgtcc | acctc  | 592  |
|    | agac | cato  | ctc ç | ggtt  | tgct  | g gt  | ctto  | tgga  | cta   | gcgc  | agc  | caga | aaga  | ac (  | ccagg | jaagga | 652  |
|    | agoo | ctcac | gt d  | ctgac | acaa  | ıg aa | cctt  | cggt  | gct:  | aacc  | cga  | gggd | ggta  | ıtg ' | tgcat | cctca  | 712  |
| 20 | gcac | ctgo  | cc a  | atccg | gcac  | c at  | ccto  | tgat  | cca   | ggga  | ictg | tgaç | caac  | ag    | ggccc | cgtgg  | 772  |
|    | ccag | gaca  | atc t | ctca  | ıccct | c ca  | igtta | aaat  | cto   | gcca  | igtt | gagt | ctgo  | cc i  | atgaa | agtag  | 832  |
|    | gtgo | tgaa  | act o | rcce  | ataa  | a to  | caca  | agta  | aga   | gttg  | ıcaa | gaaç | gago  | ca a  | aaaag | ggctg  | 892  |
|    | agct | gaat  | ga c  | ctcat | atat  | g aa  | ataa  | tttg  | , ata | atta  | ata  | taaa | ıtagç | jaa a | attta | aagtc  | 952  |
|    | tcca | gctg  | gag t | gaca  | gaaa  | a ca  | cctt  | aaaa  | ago   | tcaa  | ıgag | agag | gaaa  | igg a | aagaa | aataa  | 1012 |
| 25 | acct | ataa  | att c | gcaaa | ataa  | a ag  | catt  | gaaa  | g     |       |      |      |       |       |       |        | 1043 |

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Met

1

20 cgg cgc ctg act cgt cgg ctg gtt ctg cca gtc ttc ggg gtg ctc tgg 407
Arg Arg Leu Thr Arg Arg Leu Val Leu Pro Val Phe Gly Val Leu Trp

10 15

atc acg gtg ctg ctg ttc ttc tgg gta acc aag agg aag ttg gag gtg 455

Ile Thr Val Leu Leu Phe Phe Trp Val Thr Lys Arg Lys Leu Glu Val

25 20 25 30

|      | ccg | acg | gga | cct | gaa | gtg | cag | acc | cct  | aag | cct | tcg | gac | gct | gac | tgg  | 503 |
|------|-----|-----|-----|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|-----|------|-----|
|      | Pro | Thr | Gly | Pro | Glu | Val | Gln | Thr | Pro  | Lys | Pro | Ser | Asp | Ala | Asp | Trp. |     |
|      |     | 35  |     |     |     |     | 40  |     |      |     |     | 45  |     |     |     |      |     |
|      | gac | gac | ctg | tgg | gac | cag | ttt | gat | gag  | cgg | cgg | tat | ctg | aat | gcc | aaa  | 551 |
| 5    | Asp | Asp | Leu | Trp | Asp | Gln | Phe | Asp | Glu  | Arg | Arg | Tyr | Leu | Asn | Ala | Lys  |     |
|      | 50  |     |     |     |     | 55  |     |     |      |     | 60  |     | •   |     |     | 65   |     |
|      | aag | tgg | cgc | gtt | ggt | gac | gac | ccc | tat  | aag | ctg | tat | gct | ttc | aac | cag  | 599 |
|      | Lys | Trp | Arg | Val | Gly | Asp | Asp | Pro | Tyr  | Lys | Leu | Tyr | Ala | Phe | Asn | Gln  |     |
|      |     |     |     |     | 70  |     |     |     |      | 75  |     |     |     |     | 80  |      |     |
| LO . | cgg | gag | agt | gag | cgg | atc | tcc | agc | aat  | cgg | gcc | atc | ccg | gac | act | cgc  | 647 |
|      | Arg | Glu | Ser | Glu | Arg | Ile | Ser | Ser | Asn  | Arg | Ala | Ile | Pro | Asp | Thr | Arg  |     |
|      |     |     |     | 85  |     |     |     |     | 90   |     |     |     |     | 95  |     | 4.   |     |
|      | cat | ctg | aga | tgc | aca | ctg | ctg | gtg | tat  | tgc | acg | gac | ctt | cca | ccc | act  | 695 |
|      | His | Leu | Arg | Cys | Thr | Leu | Leu | Val | Tyr  | Cys | Thr | Asp | Leu | Pro | Pro | Thr  |     |
| 15   |     |     | 100 |     |     |     |     | 105 |      |     |     |     | 110 |     |     |      |     |
|      | agc | atc | atc | atc | acc | ttc | cac | aac | gag  | gcc | cgc | tcc | acg | ctg | ctc | agg  | 743 |
|      | Ser | Ile | Ile | Ile | Thr | Phe | His | Asn | Glu  | Ala | Arg | Ser | Thr | Leu | Leu | Arg  |     |
|      |     | 115 |     |     |     |     | 120 |     |      |     |     | 125 |     |     |     |      |     |
|      | acc | atc | cgc | agt | gta | tta | aac | cgc | acc  | cct | acg | cat | ctg | atc | cgg | gaa  | 791 |
| 20   | Thr | Ile | Arg | Ser | Val | Leu | Asn | Arg | Thr. | Pro | Thr | His | Leu | Ile | Arg | Glu  |     |
|      | 130 |     |     |     |     | 135 |     |     |      |     | 140 |     |     |     |     | 145  |     |
|      | atc | ata | tta | gtg | gat | gac | ttc | agc | aat  | gac | cct | gat | gac | tgt | aaa | cag  | 839 |
|      | Ile | Ile | Leu | Val | Asp | Asp | Phe | Ser | Asn  | Asp | Pro | Asp | Asp | Cys | Lys | Gln  |     |
|      |     |     |     |     | 150 |     |     |     |      | 155 |     |     |     |     | 160 |      |     |
| 25   | ctc | atc | aag | ttg | ccc | aag | gtg | aaa | tgc  | ttg | cqc | aat | aat | gaa | cgg | caa  | 887 |

|    | Leu | Ile  | Lys   | Leu   | Pro   | Lys   | Val   | Lys   | Cys      | Leu  | Arg   | Asn   | Asn   | Glu   | Arg   | Gln   |      |
|----|-----|------|-------|-------|-------|-------|-------|-------|----------|------|-------|-------|-------|-------|-------|-------|------|
|    |     |      |       | 165   |       |       |       |       | 170      |      |       |       |       | 175   |       |       |      |
|    | ggt | ctg  | gtc   | cgg   | tcc   | cgg   | att   | cgg   | ggc      | gct  | gac   | atc   | gcc   | cag   | ggc   | acc   | 935  |
|    | Gly | Leu  | Val   | Arg   | Ser   | Arg   | Ile   | Arg   | Gly      | Ala  | Asp   | Ile   | Ala   | Gln   | Gly   | Thr   |      |
| 5  |     |      | 180   |       |       |       |       | 185   |          |      |       |       | 190   |       |       |       |      |
|    | act | ctg  | act   | ttc   | ctc   | gac   | agc   | cac   | tgt      | gag  | gtg   | aac   | agg   | gac   | tgg   | ctc   | 983  |
|    | Thr | Leu  | Thr   | Phe   | Leu   | Asp   | Ser   | His   | Cys      | Glu  | Val   | Asn   | Arg   | Asp   | Trp   | Leu   |      |
|    |     | 195  |       |       |       |       | 200   |       |          |      | •     | 205   |       |       |       |       |      |
|    | cag | cct  | ctg   | ttg   | cac   | agg   | gtc   | aaa   | gag      | gac  | tac   | acg   | cgg   | gtg   | gtg   | tgc   | 1031 |
| 10 | Gln | Pro  | Leu   | Leu   | His   | Arg   | Val   | Lys   | Glu      | Asp  | Tyr   | Thr   | Arg   | Val   | Val   | Суѕ   |      |
| •  | 210 |      |       |       |       | 215   |       |       |          |      | 220   |       |       |       |       | 225   |      |
|    | cct | gtg  | ato   | gat   | atc   | att   | aac   | ctg   | gac      | acc  | ttc   | acc   | tac   | atc   | gag   | tct   | 1079 |
|    | Pro | Val  | Ile   | Asp   | Ile   | Ile   | Asn   | Leu   | Asp      | Thr  | Phe   | Thr   | Tyr   | Ile   | Glu   | Ser   |      |
|    |     |      |       |       | 230   |       |       |       |          | 235  |       |       |       |       | 240   |       |      |
| 15 | gcc | tcg  | gag   | ctc   | aga   | ggg   | ggg   | ttt   | gac      | tgg  | ago   | ctc   | cac   | ttc   | cag   | tgg   | 1127 |
|    | Ala | Ser  | Glu   | ı Leu | Arg   | Gly   | Gly   | Phe   | Asp      | Trp  | Ser   | Leu   | His   | Phe   | Gln   | Trp   |      |
|    |     |      |       | 245   |       |       |       |       | 250      |      |       |       |       | 255   | •     |       |      |
|    | gag | cag  | g cto | tcc   | : сса | gag   | cag   | aag   | gct      | cgg  | cgc   | ctg   | gac   | ccc   | acg   | gag   | 1175 |
|    | Glu | Glr  | n Lei | ı Ser | Pro   | Glu   | Gln   | Lys   | Ala      | Arg  | Arg   | J Leu | a Asp | Pro   | Thr   | Glu   |      |
| 20 |     |      | 260   | )     |       |       |       | 265   | <b>S</b> |      |       |       | 270   | )     |       |       |      |
|    | ccc | ato  | c agg | g act | cct   | ato   | ata   | a gct | . gga    | ggg  | g cto | c tto | gtg   | g ato | gad   | aaa   | 1223 |
|    | Pro | Ile  | e Ar  | g Thi | rPro  | Ile   | e Ile | e Ala | a Gly    | Gly  | , Tei | ı Phe | e Val | l Ile | e Asp | . Lys |      |
|    |     | 27   | 5     |       |       |       | 280   | )     |          |      |       | 285   | 5     |       |       |       |      |
|    | gct | t tg | g tt  | t gai | t tac | ct    | g ggg | g aaa | a tat    | gat  | t at  | g gad | c ato | g ga  | c ato | c tgg | 1271 |
| 25 | Ala | a Tr | p Ph  | e Ası | о Ту  | r Lei | ı Gly | y Ly: | з Туз    | : As | о Ме  | t As  | p Met | t As  | p Ile | e Trp |      |

|    | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     | 305 |      |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|    | ggt | ggg | gag | aac | ttt | gaa | atc | tcc | ttc | cga | gtg | tgg | atg | tgc | ggg | ggc | 1319 |
|    | Gly | Gly | Glu | Asn | Phe | Glu | Ile | Ser | Phe | Arg | Val | Trp | Met | Суѕ | Gly | Gly |      |
|    |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |     |      |
| 5  | agc | cta | gag | atc | gtc | ccc | tgc | agc | cga | gtg | ggg | cac | gtc | ttc | cgg | aag | 1367 |
|    | Ser | Leu | Glu | Ile | Val | Pro | Cys | Ser | Arg | Val | Gly | His | Val | Phe | Arg | Lys |      |
|    |     | •   |     | 325 | •   |     |     |     | 330 |     |     |     |     | 335 | ٠   |     |      |
|    | aag | cac | ccc | tac | gtt | ttc | cct | gat | gga | aat | gcc | aac | acg | tat | ata | aag | 1415 |
|    | Lys | His | Pro | Tyr | Val | Phe | Pro | Asp | Gly | Asn | Ala | Asn | Thr | Tyr | Ile | Lys |      |
| 10 |     |     | 340 |     |     |     |     | 345 |     |     |     |     | 350 |     |     |     |      |
|    | aac | acc | aag | cgg | aca | gct | gaa | gtg | tgg | atg | gat | gaa | tac | aag | caa | tac | 1463 |
|    | Asn | Thr | Lys | Arg | Thr | Ala | Glu | Val | Trp | Met | Asp | Glu | Tyr | Lys | Gln | Tyr |      |
|    |     | 355 |     |     |     |     | 360 |     |     |     |     | 365 |     |     |     |     |      |
|    | tat | tac | gct | gcc | cgg | cca | ttc | gcc | ctg | gag | agg | ccc | ttc | ggg | aat | gtt | 1511 |
| 15 | Tyr | Tyr | Ala | Ala | Arg | Pro | Phe | Ala | Leu | Glu | Arg | Pro | Phe | Gly | Asn | Val |      |
|    | 370 |     |     |     |     | 375 |     |     |     |     | 380 |     |     |     |     | 385 |      |
|    | gag | agc | aga | ttg | gac | ctg | agg | aag | aat | ctg | cgc | tgc | cag | agc | ttc | aag | 1559 |
|    | Glu | Ser | Arg | Leu | Asp | Leu | Arg | Lys | Asn | Leu | Arg | Cys | Gln | Ser | Phe | Lys |      |
|    |     |     |     |     | 390 |     |     |     |     | 395 |     |     |     |     | 400 |     |      |
| 20 | tgg | tac | ctg | gag | aat | atc | tac | cct | gaa | ctc | agc | atc | ccc | aag | gag | tcc | 1607 |
|    | Trp | Tyr | Leu | Glu | Asn | Ile | Tyr | Pro | Glu | Leu | Ser | Ile | Pro | Lys | Glu | Ser |      |
|    |     |     |     | 405 |     |     |     |     | 410 |     |     |     |     | 415 |     |     |      |
|    | tcc | atc | cag | aag | ggc | aat | atc | cga | cag | aga | cag | aag | tgc | ctg | gaa | tct | 1655 |
|    | Ser | Ile | Gln | Lys | Gly | Asn | Ile | Arg | Gln | Arg | Gln | Lys | Cys | Leu | Glu | Ser |      |
| 25 |     |     | 420 |     |     |     |     | 425 |     |     |     |     | 430 |     |     |     |      |

|    | •       | ,     |      |     |      |       |       |       |      |       |       |       |       |       |        |      |
|----|---------|-------|------|-----|------|-------|-------|-------|------|-------|-------|-------|-------|-------|--------|------|
|    | caa agg | cag   | aac  | aac | caa  | gaa   | acc   | cca   | aac  | cta   | aag   | ttg   | agc   | ccc   | tgt    | 1703 |
|    | Gln Arg | Gln   | Asn  | Asn | Gln  | Glu   | Thr   | Pro   | Asn  | Leu   | Lys   | Leu   | Ser   | Pro   | Cys    |      |
|    | 435     |       |      |     |      | 440   |       |       |      |       | 445   |       |       |       |        |      |
|    | gcc aag | gtc   | aaa  | ggc | gaa  | gat   | gca   | aag   | tcc  | cag   | gta   | tgg   | gcc   | ttc   | aca    | 1751 |
| 5  | Ala Lys | Val   | Lys  | Gly | Glu  | Asp   | Ala   | Lys   | Ser  | Gln   | Val   | Trp   | Ala   | Phe   | Thr    |      |
|    | 450     |       |      |     | 455  |       |       |       |      | 460   |       |       |       |       | 465    |      |
|    | tac acc | cag   | cag  | atc | ctc  | cag   | gag   | gag   | ctg  | tgc   | ctg   | tca   | gtc   | atc   | acc    | 1799 |
|    | Tyr Thr | Gln   | Gln  | Ile | Leu  | Gln   | Glu   | Glu   | Leu  | Cys   | Leu   | Ser   | Val   | Ile   | Thr    |      |
|    | -       |       |      | 470 |      |       |       |       | 475  |       |       |       |       | 480   |        |      |
| 10 | ttg ttc | cct   | ggc  | gcc | cca  | gtg   | gtt   | ctt   | gtc  | ctt   | tgc   | aag   | aat   | gga   | gat    | 1847 |
|    | Leu Phe | Pro   | Gly  | Ala | Pro  | Val   | Val   | Leu   | Val  | Leu   | Cys   | Lys   | Asn   | Gly   | Asp    |      |
|    |         |       | 485  |     |      |       |       | 490   |      |       |       |       | 495   |       |        |      |
|    | gac cga | cag   | caa  | tgg | acc  | aaa   | act   | ggt   | tcc  | cac   | atc   | gag   | cac   | ata   | gca    | 1895 |
|    | Asp Arg | Gln   | Gln  | Trp | Thr  | Lys   | Thr   | Gly   | Ser  | His   | Ile   | Glu   | His   | Ile   | Ala    |      |
| 15 |         | 500   |      |     |      |       | 505   |       |      |       |       | 510   |       | •     |        |      |
|    | tcc cac | ctc   | tgc  | ctc | gat  | aca   | gat   | atg   | ttc  | ggt   | gat   | ggc   | acc   | gag   | aac    | 1943 |
|    | Ser His | Leu   | Cys  | Leu | Asp  | Thr   | Asp   | Met   | Phe  | Gly   | Asp   | Gly   | Thr   | Glu   | Asn    |      |
|    | 515     |       |      |     |      | 520   |       |       |      |       | 525   |       |       |       |        |      |
|    | ggc aag | gaa   | atc  | gtc | gtc  | aac   | сса   | tgt   | gag  | tcc   | tca   | ctc   | atg   | agc   | cag    | 1991 |
| 20 | Gly Lys | Glu   | Ile  | Val | Val  | Asn   | Pro   | Cys   | Glu  | Ser   | Ser   | Leu   | Met   | Ser   | Gln    |      |
|    | 530     |       |      |     | 535  |       |       |       |      | 540   |       |       |       |       | 545    |      |
|    | cac tgg | gac   | atg  | gtg | agc  | tct   | tga   | ggad  | ecct | ige d | cagaa | ıgcaç | jc aa | agggo | catq   | 2045 |
|    | His Trp |       |      |     |      |       |       |       |      |       |       |       |       |       |        |      |
|    |         |       |      | 550 |      |       |       |       |      |       |       |       |       |       |        |      |
| 25 | gggtggt | gct t | ccct |     | c ac | gaaca | agact | . qqa | aact | agaa  | caaa  | aaaa  | aq o  | ctac  | caacca | 2105 |

5

| cctcagacat | cctggactgg | gaggtggagg  | cagagccccc | caggacagga | gcaactgtct | 2165 |
|------------|------------|-------------|------------|------------|------------|------|
| cagggaggac | agaggaaaac | atcacaagcc  | aatggggctc | aaagacaaat | cccacatgtt | 2225 |
| ctcaaggccg | ttaagttcca | gtcctggcca  | gtcattccct | gattggtatc | tggagacaga | 2285 |
| aacctaatgg | gaagtgttta | ttgttccttt  | tcctacaaag | gaagcagtct | ctggaggcca | 2345 |
| gaaagaaaag | ccttcttttt | cactaggcca  | ggactacatt | gagagatgaa | gaatggaggt | 2405 |
| totttccaaa | agaaataaa  | g agaaactta | ια         |            |            | 2435 |